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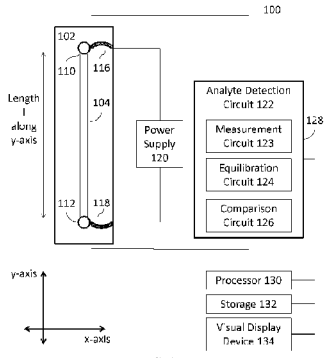

FIG. 1A

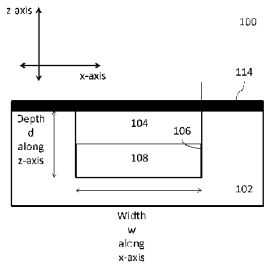

FIG. 1B

(57) Abstract: Embodiments provide analyte detection systems and methods for detecting the presence of one or more analytes in one or more samples. In a detection method, a sample and a sensor compound is introduced into a channel. A first potential difference is applied across the length of the channel in a first direction, and a first electrical property value is detected. Subsequently, a second potential difference is applied across the length of the channel in a second opposite direction, and a second electrical property value is detected. Presence or absence of an analyte in the channel is determined based on a comparison between the first and second electrical property values.

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METHODS AND SYSTEMS FOR DETECTION OF ANALYTES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority from: U.S. Patent Application No. 14/507,825, filed October 6, 2014, entitled "SYSTEM FOR DETECTION OF ANALYTES"; U.S. Patent Application No. 14/507,828, filed October 6, 2014, entitled "METHOD FOR DETECTION OF ANALYTES"; U.S. Patent Application No. 14/507,818, filed October 6, 2014 entitled "SYSTEM AND METHOD FOR DETECTION OF MERCURY"; U.S. Patent Application No. 14/507,820, filed October 6, 2014 entitled "SYSTEM AND METHOD FOR DETECTION OF SILVER"; and U.S. Patent Application No. 14/535,378 filed November 7, 2014, entitled "SYSTEM AND METHOD FOR DETECTION OF NUCLEIC ACIDS", each of which is incorporated by reference in its entirety.

BACKGROUND

[0002] Sensitive and selective detection of chemical and biological analytes has important implications for medical and environmental testing and research. Hospitals and laboratories, for example, routinely test biological samples to detect potentially toxic substances, such as mercury and silver, in heavy metal poisoning diagnosis. Similarly, measurement of biomolecules, such as nucleic acids, is a foundation of modern medicine and is used in medical research, diagnostics, therapy and drug development.

[0003] Nanopore sequencing technology is a conventional method of detecting nucleic acid molecules. The concept of nanopore sequencing utilizes a nanopore aperture, which is a small hole or pore that extends transversely through a lipid bilayer membrane, i.e., through the depth or thickness dimension of the membrane. Nanopore sequencing involves causing a nucleotide to travel through a nanopore in the membrane, i.e., to travel between the top surface and the bottom surface of the membrane along the depth or thickness dimension of the membrane. A potential difference may be applied across the depth or thickness dimension of the membrane to force the nucleotide to travel through the nanopore. Physical changes in the environment of the nucleotide (for example, electric current passing through the nanopore) are detected as the nucleotide traverses through the nanopore. Based on the detected changes in the electrical current, the nucleotide may be identified and sequenced.

[0004] Areas for improving and broadening the scope of conventional systems and techniques of nucleic acid detection have been identified, and technical solutions have been implemented in exemplary embodiments.

SUMMARY

[0004a] In one aspect, the present invention provides a method for detecting the presence or absence of an analyte in a sample, the method comprising:

introducing a sample into a channel, the channel having a length and a width, the length substantially greater than the width;

introducing a solution comprising a dissolved sensor compound into the channel, wherein the sensor compound is allowed to flow along the length of the channel;

measuring an electrical property value of an electrical property along at least a portion of the length of the channel after the sample and sensor compound are introduced into the channel;

accessing a reference electrical property value, wherein the reference electrical property value of an electrical property of the channel along at least a portion of the length of the channel is obtained prior to introduction of the sample into the channel;

comparing the measured electrical property value and the reference electrical property value; and

determining whether an aggregate is present in an inner space of the channel based on the comparison between the measured electrical property value and the reference electrical property value, wherein the aggregate is formed in the inner space of the channel by an interaction between the analyte and the sensor compound, thereby determining whether the analyte is present in the channel.

[0004b] In another aspect, the present invention provides a detection system for detecting an analyte in the presence of a sensor compound, comprising:

a substrate having at least one channel, wherein the at least one channel has a length and a width, wherein the length is substantially greater than the width, and comprises a solution comprising a dissolved sensor compound, wherein the sensor compound is allowed

to flow along the length of the channel, and wherein an interaction between the analyte and the sensor compound results in formation of an aggregate;

a first port in fluid communication with a first end section of the at least one channel;

a second port in fluid communication with a second end section of the at least one channel;

a first electrode electrically connected at the first end section of the at least one channel and a second electrode electrically connected at the second end section of the at least one channel, the first and second electrodes electrically connected to their respective first and second end sections of the at least one channel to form a channel circuit, the channel circuit having electrical properties and configured such that when an electrically conductive fluid is present in the at least one channel, the electrically conductive fluid alters the electrical properties of the channel circuit; and

an analyte detection circuit in electrical communication with the first and second electrodes, the analyte detection circuit including a measurement circuit in electrical communication with the first and second electrode, the measurement circuit having a measurement circuit output, the measurement circuit output including one or more values indicative of one or more electrical properties of the channel circuit, the analyte detection circuit including a memory in electrical communication with the measurement circuit output and configured to store the one or more values indicative of the one or more electrical properties of the channel circuit including at least a first value of an electrical property of the channel circuit and a second value of the electrical property of the channel circuit, the analyte detection circuit further including a comparison circuit in electrical communication with the memory and having as inputs the at least first and second values, the comparison circuit configured to provide a comparison circuit output based at least in part on the at least first and/or second values, the comparison circuit output indicative of whether the aggregate is present in the at least one channel.

[0004c] In the description in this specification reference may be made to subject matter which is not within the scope of the appended claims. That subject matter should be readily identifiable by a person skilled in the art and may assist in putting into practice the invention as defined in the appended claims.

[0005] In accordance with one exemplary embodiment, a method is provided for detecting the presence or absence of an analyte in a sample. The method includes introducing a sample into a channel, the channel having a length and a width, the length substantially greater than the width; measuring an electrical property value of an electrical property along at least a portion of the length of the channel after the sample is introduced into the channel; accessing a reference electrical property value, the reference electrical property value associated with the electrical property of the channel along at least a portion of the length of the channel prior to introduction of the sample into the channel; comparing the measured electrical property value and the reference electrical property value; and determining whether an analyte is present in the channel based on the comparison between the measured electrical property value and the reference electrical property value.

[0006] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of an analyte in a sample. The method includes measuring one or more electrical properties of a channel along at least a portion of the length of the channel, the channel having a length and a width, the length substantially greater than the width; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; introducing a sample into the channel; measuring the one or more electrical properties of the channel along the same portion of the length of the channel that was measured in the first measuring step with the sample in the channel; determining a sample channel electrical property value based on the one or more electrical properties of the channel measured with the sample in the channel; determining any differences between the sample channel electrical property value and the reference channel electrical property value; and determining whether an analyte is present in the channel based on the differences, if any, between the sample channel electrical property value and the reference channel electrical property value.

[0007] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of an analyte in a sample. The method includes introducing a sample and a sensor compound into a channel, the channel having a length and a width, the length substantially greater than the width; measuring an electrical property value along at least a portion of the length of the channel after the sample and the sensor compound are introduced into the channel; accessing a reference electrical property value

from memory, the reference electrical property value associated with at least a portion of the length of the channel; determining any differences between the measured electrical property value and the reference electrical property value; and determining whether an analyte is present in the channel based on the differences, if any, between the measured electrical property value and the reference electrical property value.

[0008] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of an analyte in a sample. The method includes introducing a sensor compound into a channel, the channel having a length and a width, the length being substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; introducing a sample into the channel; measuring the one or more electrical properties of the channel along at least the portion of the length of the channel after the sample and the sensor compound are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the sensor compound and the sample are introduced into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether an analyte is present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0009] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of an analyte in a sample. The method includes introducing a sensor compound into a channel, the channel having a length and a width, the length being substantially greater than the width; introducing a sample into the channel; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the sample and the sensor compound are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the sensor compound and the sample are introduced into the channel; accessing a reference channel electrical property value, the reference channel electrical property value measured prior to introduction of both the sensor compound and the sample into the channel; determining any differences between the reference channel

electrical property value and the electrical property value; and determining whether an analyte is present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0010] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of an analyte in a sample. The method includes introducing a sample into a channel, the channel having a length and a width, the length being substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; introducing a sensor compound into the channel; measuring the one or more electrical properties of the channel along at least the portion of the length of the channel after the sample and the sensor compound are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the sensor compound and the sample are introduced into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether an analyte is present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0011] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of an analyte in a sample. The method includes introducing a sample into a channel, the channel having a length and a width, the length being substantially greater than the width; introducing a sensor compound into the channel; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the sample and the sensor compound are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the sensor compound and the sample are introduced into the channel; accessing a reference channel electrical property value, the reference channel electrical property value measured prior to introduction of both the sensor compound and the sample into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether an

analyte is present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0012] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of an analyte in a sample. The method includes coating at least a portion of an inner surface of a channel with a sensor compound, the channel having a length and a width, the length substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the channel is coated with the sensor compound; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; and storing the reference channel electrical property value for use in determining whether or not an analyte is present in a sample introduced in the channel.

[0013] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of an analyte in a sample. The method includes introducing a sample and a sensor compound into a channel, the channel having a length and a width, the length substantially greater than the width. The method also includes applying a first potential difference across the length of the channel in a first direction along the length of the channel. The method also includes measuring a first electrical property value of an electrical property along at least a portion of the length of the channel while the first potential difference is applied. The method also includes applying a second potential difference across the length of the channel in a second direction along the length of the channel, the second direction opposite to the first direction. The method also includes measuring a second electrical property value of the electrical property along at least the portion of the length of the channel while the second potential difference is applied. The method also includes comparing the first and second electrical property values. The method also includes determining whether an analyte is present in the channel based on the comparison between the first and second electrical property values.

[0014] In accordance with one exemplary embodiment, a detection system is provided. The detection system includes a substrate, the substrate having at least one channel, the at least one channel having a length and a width, the length substantially greater than the width. The detection system also includes a first port in fluid communication with a first end

section of the at least one channel, and a second port in fluid communication with a second end section of the at least one channel. The detection system also includes a first electrode electrically connected at the first end section of the at least one channel and a second electrode electrically connected at the second end section of the at least one channel. The first and second electrodes are electrically connected to their respective first and second end sections of the at least one channel to form a channel circuit. The channel circuit has electrical properties and is configured such that when an electrically conductive fluid is present in the at least one channel, the electrically conductive fluid alters the electrical properties of the channel circuit. The detection system also includes an analyte detection circuit in electrical communication with the first and second electrodes. The analyte detection circuit includes a measurement circuit in electrical communication with the first and second electrode. The measurement circuit has a measurement circuit output, the measurement circuit output including one or more values indicative of one or more electrical properties of the channel circuit. The analyte detection circuit also includes a memory in electrical communication with the measurement circuit output and configured to store the one or more values indicative of the one or more electrical properties of the channel circuit including at least a first value of an electrical property of the channel circuit and a second value of the electrical property of the channel circuit. The analyte detection circuit further includes a comparison circuit in electrical communication with the memory and having as inputs the at least first and second values. The comparison circuit is configured to provide a comparison circuit output based at least in part on the at least first and/or second values. The comparison circuit output is indicative of whether an analyte is present in the at least one channel.

[0015] In accordance with another exemplary embodiment, a detection system is provided. The detection system includes a substrate, the substrate having at least one channel, the at least one channel having a length and a width, the length substantially greater than the width. The detection system also includes a first port in fluid communication with a first end section of the at least one channel, and a second port in fluid communication with a second end section of the at least one channel. The detection system also includes a first electrode electrically connected at the first end section of the at least one channel and a second electrode electrically connected at the second end section of the at least one channel. The first and second electrodes are electrically connected to their respective first and second

end sections of the at least one channel such that when an electrically conductive fluid is present in the at least one channel, the electrically conductive fluid completes an electrical circuit between the first and second electrodes. The detection system also includes analyte detection circuitry in electrical communication with the first and second electrodes. The analyte detection circuitry is configured to measure one or more electrical properties between the first and second electrodes. The analyte detection circuitry includes a memory, the memory configured to store a measured electrical property value. The analyte detection circuitry further includes a comparison circuit configured to detect presence of an analyte in the at least one channel based on the measured electrical property value.

[0016] In accordance with another exemplary embodiment, a detection system is provided. The detection system includes means for accommodating a fluid flow, means for introducing a fluid at a first terminal end of the means for accommodating the fluid flow, means for outputting the fluid at a second terminal end of the means for accommodating the fluid flow, means for detecting first and second values of an electrical property of the fluid between the first and second terminal ends of the means for accommodating the fluid flow, and means for determining whether an analyte is present in the fluid based on a difference between the first and second values of the electrical property.

[0017] In accordance with one exemplary embodiment, a method is provided for detecting the presence or absence of mercury ions in a sample. The method includes introducing a sample into a channel, the channel having a length and a width, the length substantially greater than the width; measuring an electrical property value of an electrical property along at least a portion of the length of the channel after the sample is introduced into the channel; accessing a reference electrical property value, the reference electrical property value associated with the electrical property of the channel along at least a portion of the length of the channel prior to introduction of the sample into the channel; comparing the measured electrical property value and the reference electrical property value; and determining whether mercury ions are present in the channel based on the comparison between the measured electrical property value and the reference electrical property value.

[0018] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of mercury ions in a sample. The method includes measuring one or more electrical properties of a channel along at least a portion of the length

of the channel, the channel having a length and a width, the length substantially greater than the width; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; introducing a sample into the channel; measuring the one or more electrical properties of the channel along the same portion of the length of the channel that was measured in the first measuring step with the sample in the channel; determining a sample channel electrical property value based on the one or more electrical properties of the channel measured with the sample in the channel; determining any differences between the sample channel electrical property value and the reference channel electrical property value; and determining whether mercury ions are present in the channel based on the differences, if any, between the sample channel electrical property value and the reference channel electrical property value.

[0019] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of mercury ions in a sample. The method includes introducing a sample and TPET2 molecules into a channel, the channel having a length and a width, the length substantially greater than the width; measuring an electrical property value along at least a portion of the length of the channel after the sample and the TPET2 molecules are introduced into the channel; accessing a reference electrical property value from memory, the reference electrical property value associated with at least a portion of the length of the channel; determining any differences between the measured electrical property value and the reference electrical property value; and determining whether mercury ions are present in the channel based on the differences, if any, between the measured electrical property value and the reference electrical property value.

[0020] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of mercury ions in a sample. The method includes introducing TPET2 molecules into a channel, the channel having a length and a width, the length being substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; introducing a sample into the channel; measuring the one or more electrical properties of the channel along at least the portion of the length of the channel after the sample and the TPET2 molecules are introduced into the

channel; determining an electrical property value based on the one or more electrical properties measured after the TPET2 molecules and the sample are introduced into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether mercury ions are present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0021] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of mercury ions in a sample. The method includes introducing TPET2 molecules into a channel, the channel having a length and a width, the length being substantially greater than the width; introducing a sample into the channel; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the sample and the TPET2 molecules are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the TPET2 molecules and the sample are introduced into the channel; accessing a reference channel electrical property value, the reference channel electrical property value measured prior to introduction of both the TPET2 molecules and the sample into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether mercury ions are present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0022] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of mercury ions in a sample. The method includes introducing a sample into the channel, the channel having a length and a width, the length being substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; introducing TPET2 molecules into a channel; measuring the one or more electrical properties of the channel along at least the portion of the length of the channel after the sample and the TPET2 molecules are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the TPET2 molecules and the sample are introduced into the

channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether mercury ions are present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0023] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of mercury ions in a sample. The method includes introducing a sample into the channel, the channel having a length and a width, the length being substantially greater than the width; introducing TPET2 molecules into a channel; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the sample and the TPET2 molecules are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the TPET2 molecules and the sample are introduced into the channel; accessing a reference channel electrical property value, the reference channel electrical property value measured prior to introduction of both the TPET2 molecules and the sample into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether mercury ions are present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0024] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of mercury ions in a sample. The method includes coating at least a portion of an inner surface of a channel with TPET2 molecules, the channel having a length and a width, the length substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the channel is coated with the TPET2 molecules; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; and storing the reference channel electrical property value for use in determining whether or not mercury ions are present in a sample introduced in the channel.

[0025] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of mercury ions in a sample. The method includes introducing a sample and TPET2 molecules into a channel, the channel having a length and a

width, the length substantially greater than the width. The method also includes applying a first potential difference across the length of the channel in a first direction along the length of the channel. The method also includes measuring a first electrical property value of an electrical property along at least a portion of the length of the channel while the first potential difference is applied. The method also includes applying a second potential difference across the length of the channel in a second direction along the length of the channel, the second direction opposite to the first direction. The method also includes measuring a second electrical property value of the electrical property along at least the portion of the length of the channel while the second potential difference is applied. The method also includes comparing the first and second electrical property values. The method also includes determining whether mercury ions are present in the channel based on the comparison between the first and second electrical property values.

[0026] In accordance with another exemplary embodiment, a mercury detection system is provided. The system includes a substrate, the substrate having at least one channel, the at least one channel having a length and a width, the length substantially greater than the width; a first port in fluid communication with a first end section of the at least one channel; and a second port in fluid communication with a second end section of the at least one channel. The system also includes a first electrode electrically connected at the first end section of the at least one channel and a second electrode electrically connected at the second end section of the at least one channel, the first and second electrodes electrically connected to their respective first and second end sections of the at least one channel to form a channel circuit, the channel circuit having electrical properties and configured such that when an electrically conductive fluid is present in the at least one channel, the electrically conductive fluid alters the electrical properties of the channel circuit. The system further includes a mercury detection circuit in electrical communication with the first and second electrodes, the mercury detection circuit including a measurement circuit in electrical communication with the first and second electrode, the measurement circuit having a measurement circuit output, the measurement circuit output including one or more values indicative of one or more electrical properties of the channel circuit, the mercury detection circuit including a memory in electrical communication with the measurement circuit output and configured to store the one or more values indicative of the one or more electrical properties of the channel

circuit including at least a first value of an electrical property of the channel circuit and a second value of the electrical property of the channel circuit, the mercury detection circuit further including a comparison circuit in electrical communication with the memory and having as inputs the at least first and second values, the comparison circuit configured to provide a comparison circuit output based at least in part on the at least first and/or second values, the comparison circuit output indicative of whether mercury ions are present in the at least one channel.

[0027] In accordance with another exemplary embodiment, a mercury detection system is provided. The system includes means for accommodating a fluid flow; means for introducing a fluid at a first terminal end of the means for accommodating the fluid flow; means for outputting the fluid at a second terminal end of the means for accommodating the fluid flow; means for detecting first and second values of an electrical property of the fluid between the first and second terminal ends of the means for accommodating the fluid flow; and means for determining whether mercury ions are present in the fluid based on a difference between the first and second values of the electrical property.

[0028] In accordance with one exemplary embodiment, a method is provided for detecting the presence or absence of silver ions in a sample. The method includes introducing a sample into a channel, the channel having a length and a width, the length substantially greater than the width; measuring an electrical property value of an electrical property along at least a portion of the length of the channel after the sample is introduced into the channel; accessing a reference electrical property value, the reference electrical property value associated with the electrical property of the channel along at least a portion of the length of the channel prior to introduction of the sample into the channel; comparing the measured electrical property value and the reference electrical property value; and determining whether silver ions are present in the channel based on the comparison between the measured electrical property value and the reference electrical property value.

[0029] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of silver ions in a sample. The method includes measuring one or more electrical properties of a channel along at least a portion of the length of the channel, the channel having a length and a width, the length substantially greater than the width; determining a reference channel electrical property value based on the one or more

electrical properties of the channel measured during the previous measuring step; introducing a sample into the channel; measuring the one or more electrical properties of the channel along the same portion of the length of the channel that was measured in the first measuring step with the sample in the channel; determining a sample channel electrical property value based on the one or more electrical properties of the channel measured with the sample in the channel; determining any differences between the sample channel electrical property value and the reference channel electrical property value; and determining whether silver ions are present in the channel based on the differences, if any, between the sample channel electrical property value and the reference channel electrical property value.

[0030] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of silver ions in a sample. The method includes introducing a sample and TPEA2 molecules into a channel, the channel having a length and a width, the length substantially greater than the width; measuring an electrical property value along at least a portion of the length of the channel after the sample and the TPEA2 molecules are introduced into the channel; accessing a reference electrical property value from memory, the reference electrical property value associated with at least a portion of the length of the channel; determining any differences between the measured electrical property value and the reference electrical property value; and determining whether silver ions are present in the channel based on the differences, if any, between the measured electrical property value and the reference electrical property value.

[0031] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of silver ions in a sample. The method includes introducing TPEA2 molecules into a channel, the channel having a length and a width, the length being substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; introducing a sample into the channel; measuring the one or more electrical properties of the channel along at least the portion of the length of the channel after the sample and the TPEA2 molecules are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the TPEA2 molecules and the sample are introduced into the

channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether silver ions are present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0032] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of silver ions in a sample. The method includes introducing TPEA2 molecules into a channel, the channel having a length and a width, the length being substantially greater than the width; introducing a sample into the channel; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the sample and the TPEA2 molecules are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the TPEA2 molecules and the sample are introduced into the channel; accessing a reference channel electrical property value, the reference channel electrical property value measured prior to introduction of both the TPEA2 molecules and the sample into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether silver ions are present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0033] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of silver ions in a sample. The method includes introducing a sample into the channel, the channel having a length and a width, the length being substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; introducing TPEA2 molecules into a channel; measuring the one or more electrical properties of the channel along at least the portion of the length of the channel after the sample and the TPEA2 molecules are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the TPEA2 molecules and the sample are introduced into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether silver ions are present in the

channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0034] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of silver ions in a sample. The method includes introducing a sample into the channel, the channel having a length and a width, the length being substantially greater than the width; introducing TPEA2 molecules into a channel; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the sample and the TPEA2 molecules are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the TPEA2 molecules and the sample are introduced into the channel; accessing a reference channel electrical property value, the reference channel electrical property value measured prior to introduction of both the TPEA2 molecules and the sample into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether silver ions are present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0035] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of silver ions in a sample. The method includes coating at least a portion of an inner surface of a channel with TPEA2 molecules, the channel having a length and a width, the length substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the channel is coated with the TPEA2 molecules; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; and storing the reference channel electrical property value for use in determining whether or not silver ions are present in a sample introduced in the channel.

[0036] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of silver ions in a sample. The method includes introducing a sample and TPEA2 molecules into a channel, the channel having a length and a width, the length substantially greater than the width. The method also includes applying a first potential difference across the length of the channel in a first direction along the length

of the channel. The method also includes measuring a first electrical property value of an electrical property along at least a portion of the length of the channel while the first potential difference is applied. The method also includes applying a second potential difference across the length of the channel in a second direction along the length of the channel, the second direction opposite to the first direction. The method also includes measuring a second electrical property value of the electrical property along at least the portion of the length of the channel while the second potential difference is applied. The method also includes comparing the first and second electrical property values. The method also includes determining whether silver ions are present in the channel based on the comparison between the first and second electrical property values.

[0037] In accordance with another exemplary embodiment, a silver detection system is provided. The system includes a substrate, the substrate having at least one channel, the at least one channel having a length and a width, the length substantially greater than the width; a first port in fluid communication with a first end section of the at least one channel; and a second port in fluid communication with a second end section of the at least one channel. The system also includes a first electrode electrically connected at the first end section of the at least one channel and a second electrode electrically connected at the second end section of the at least one channel, the first and second electrodes electrically connected to their respective first and second end sections of the at least one channel to form a channel circuit, the channel circuit having electrical properties and configured such that when an electrically conductive fluid is present in the at least one channel, the electrically conductive fluid alters the electrical properties of the channel circuit. The system further includes a silver detection circuit in electrical communication with the first and second electrodes, the silver detection circuit including a measurement circuit in electrical communication with the first and second electrode, the measurement circuit having a measurement circuit output, the measurement circuit output including one or more values indicative of one or more electrical properties of the channel circuit, the silver detection circuit including a memory in electrical communication with the measurement circuit output and configured to store the one or more values indicative of the one or more electrical properties of the channel circuit including at least a first value of an electrical property of the channel circuit and a second value of the electrical property of the channel circuit, the silver detection circuit further including a

comparison circuit in electrical communication with the memory and having as inputs the at least first and second values, the comparison circuit configured to provide a comparison circuit output based at least in part on the at least first and/or second values, the comparison circuit output indicative of whether an silver is present in the at least one channel.

[0038] In accordance with another exemplary embodiment, a silver detection system is provided. The system includes means for accommodating a fluid flow; means for introducing a fluid at a first terminal end of the means for accommodating the fluid flow; means for outputting the fluid at a second terminal end of the means for accommodating the fluid flow; means for detecting first and second values of an electrical property of the fluid between the first and second terminal ends of the means for accommodating the fluid flow; and means for determining whether silver is present in the fluid based on a difference between the first and second values of the electrical property.

[0039] In accordance with one exemplary embodiment, a method is provided for detecting the presence or absence of a nucleic acid in a sample. The method includes introducing a sample into a channel, the channel having a length and a width, the length substantially greater than the width; measuring an electrical property value of an electrical property along at least a portion of the length of the channel after the sample is introduced into the channel; accessing a reference electrical property value, the reference electrical property value associated with the electrical property of the channel along at least a portion of the length of the channel prior to introduction of the sample into the channel; comparing the measured electrical property value and the reference electrical property value; and determining whether the nucleic acid is present in the channel based on the comparison between the measured electrical property value and the reference electrical property value.

[0040] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of a nucleic acid in a sample. The method includes measuring one or more electrical properties of a channel along at least a portion of the length of the channel, the channel having a length and a width, the length substantially greater than the width; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; introducing a sample into the channel; measuring the one or more electrical properties of the channel along the same portion of the length of the channel that was measured in the first measuring

step with the sample in the channel; determining a sample channel electrical property value based on the one or more electrical properties of the channel measured with the sample in the channel; determining any differences between the sample channel electrical property value and the reference channel electrical property value; and determining whether a nucleic acid is present in the channel based on the differences, if any, between the sample channel electrical property value and the reference channel electrical property value.

[0041] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of a nucleic acid in a sample. The method includes introducing a sample and one or more nucleic acid probes into a channel, the channel having a length and a width, the length substantially greater than the width; measuring an electrical property value along at least a portion of the length of the channel after the sample and the nucleic acid probes are introduced into the channel; accessing a reference electrical property value from memory, the reference electrical property value associated with at least a portion of the length of the channel; determining any differences between the measured electrical property value and the reference electrical property value; and determining whether the nucleic acid probe is present in the channel based on the differences, if any, between the measured electrical property value and the reference electrical property value.

[0042] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of a nucleic acid probe in a sample. The method includes introducing one or more nucleic acid probes into a channel, the channel having a length and a width, the length being substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; introducing a sample into the channel; measuring the one or more electrical properties of the channel along at least the portion of the length of the channel after the sample and the one or more nucleic acid probes are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the one or more nucleic acid probes and the sample are introduced into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether

the nucleic acid is present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0043] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of a nucleic acid in a sample. The method includes introducing one or more nucleic acid probes into a channel, the channel having a length and a width, the length being substantially greater than the width; introducing a sample into the channel; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the sample and the one or more nucleic acid probes are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the one or more nucleic acid probes and the sample are introduced into the channel; accessing a reference channel electrical property value, the reference channel electrical property value measured prior to introduction of both the one or more nucleic acid probes and the sample into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether the nucleic acid is present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0044] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of a nucleic acid in a sample. The method includes introducing a sample into a channel, the channel having a length and a width, the length being substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; introducing one or more nucleic acid probes into the channel; measuring the one or more electrical properties of the channel along at least the portion of the length of the channel after the sample and the one or more nucleic acid probes are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the one or more nucleic acid probes and the sample are introduced into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether the nucleic acid is present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0045] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of a nucleic acid in a sample. The method includes introducing a sample into a channel, the channel having a length and a width, the length being substantially greater than the width; introducing one or more nucleic acid probes into the channel; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the sample and the one or more nucleic acid probes are introduced into the channel; determining an electrical property value based on the one or more electrical properties measured after the one or more nucleic acid probes and the sample are introduced into the channel; accessing a reference channel electrical property value, the reference channel electrical property value measured prior to introduction of both the one or more nucleic acid probes and the sample into the channel; determining any differences between the reference channel electrical property value and the electrical property value; and determining whether the nucleic acid is present in the channel based on the differences, if any, between the reference channel electrical property value and the electrical property value.

[0046] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of a nucleic acid in a sample. The method includes coating at least a portion of an inner surface of a channel with one or more nucleic acid probes, the channel having a length and a width, the length substantially greater than the width; measuring one or more electrical properties of the channel along at least a portion of the length of the channel after the channel is coated with the one or more nucleic acid probes; determining a reference channel electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step; and storing the reference channel electrical property value for use in determining whether or not the nucleic acid is present in a sample introduced in the channel.

[0047] In accordance with another exemplary embodiment, a method is provided for detecting the presence or absence of a nucleic acid in a sample. The method includes introducing a sample and one or more nucleic acid probes into a channel, the channel having a length and a width, the length substantially greater than the width. The method also includes applying a first potential difference across the length of the channel in a first direction along the length of the channel. The method also includes measuring a first electrical property value of an electrical property along at least a portion of the length of the

channel while the first potential difference is applied. The method also includes applying a second potential difference across the length of the channel in a second direction along the length of the channel, the second direction opposite to the first direction. The method also includes measuring a second electrical property value of the electrical property along at least the portion of the length of the channel while the second potential difference is applied. The method also includes comparing the first and second electrical property values. The method also includes determining whether a nucleic acid is present in the channel based on the comparison between the first and second electrical property values.

[0048] In accordance with another exemplary embodiment, a nucleic acid detection system is provided. The system includes a substrate, the substrate having at least one channel, the at least one channel having a length and a width, the length substantially greater than the width; a first port in fluid communication with a first end section of the at least one channel; and a second port in fluid communication with a second end section of the at least one channel. The system also includes a first electrode electrically connected at the first end section of the at least one channel and a second electrode electrically connected at the second end section of the at least one channel, the first and second electrodes electrically connected to their respective first and second end sections of the at least one channel to form a channel circuit, the channel circuit having electrical properties and configured such that when an electrically conductive fluid is present in the at least one channel, the electrically conductive fluid alters the electrical properties of the channel circuit. The system further includes a detection circuit in electrical communication with the first and second electrodes, the detection circuit including a measurement circuit in electrical communication with the first and second electrode, the measurement circuit having a measurement circuit output, the measurement circuit output including one or more values indicative of one or more electrical properties of the channel circuit, the detection circuit including a memory in electrical communication with the measurement circuit output and configured to store the one or more values indicative of the one or more electrical properties of the channel circuit including at least a first value of an electrical property of the channel circuit and a second value of the electrical property of the channel circuit, the detection circuit further including a comparison circuit in electrical communication with the memory and having as inputs the at least first and second values, the comparison circuit configured to provide a comparison circuit output

based at least in part on the at least first and/or second values, the comparison circuit output indicative of whether a nucleic acid is present in the at least one channel.

[0049] In accordance with another exemplary embodiment, a nucleic acid detection system is provided. The system includes means for accommodating a fluid flow; means for introducing a fluid at a first terminal end of the means for accommodating the fluid flow; means for outputting the fluid at a second terminal end of the means for accommodating the fluid flow; means for detecting first and second values of an electrical property of the fluid between the first and second terminal ends of the means for accommodating the fluid flow; and means for determining whether a nucleic acid is present in the fluid based on a difference between the first and second values of the electrical property.

BRIEF DESCRIPTION OF THE DRAWINGS

[0050] The foregoing and other objects, aspects, features, and advantages of exemplary embodiments will become more apparent and may be better understood by referring to the following description taken in conjunction with the accompanying drawings.

[0051] Figure 1A illustrates a top view of an exemplary detection system including a single channel.

[0052] Figure 1B illustrates a cross-sectional side view of the exemplary detection system of Figure 1A.

[0053] Figure 2 illustrates a schematic cross-sectional side view of the channel of the exemplary detection system of Figure 1A, showing aggregate particles and an electrical double layer (EDL).

[0054] Figure 3 illustrates a top view of an exemplary detection system including multiple channels.

[0055] Figure 4 illustrates a top view of another exemplary detection system including multiple channels.

[0056] Figure 5 is a schematic representing exemplary ions in an exemplary detection system.

[0057] Figures 6A and 6B are graphs illustrating exemplary conductivity values measured in a channel at different concentrations of an exemplary analyte.

[0058] Figures 7A, 7B, 8A, 8B, and 9-16 are flowcharts illustrating exemplary methods for detecting an analyte (e.g., mercury or silver) in a sample.

[0059] Figures 17A and 17B are flowcharts illustrating an exemplary method for detecting a solvent in a sample.

[0060] Figure 18 is a block diagram of an exemplary processing or computing device that may be used to implement and execute exemplary computer-executable methods.

[0061] Figures 19A, 19B and 20-27 are flowcharts illustrating exemplary methods for detecting nucleic acid in a sample.

[0062] Figure 28 is a schematic illustrating formation of a nucleic acid aggregate during detection of a nuclei acid.

[0063] Figures 29A and 29B are flowcharts illustrating another exemplary method for detecting nucleic acid in a sample.

[0064] The accompanying drawings are not intended to be drawn to scale.

DETAILED DESCRIPTION

[0065] Areas for improving conventional systems and techniques of analyte (e.g., mercury, silver, or nucleic acids and nucleotides) detection have been identified and technical solutions have been implemented in exemplary embodiments. Exemplary embodiments provide analyte (e.g., mercury, silver, or nucleic acids) detection systems and techniques that couple knowledge of nano and microfluidic surface chemistry, electrokinetics and fluid dynamics to provide novel functional capabilities. Compared to conventional techniques such as nanopore technology, embodiments provide improved dimensional precision and control, resulting in new functionality and enhanced device performance.

[0066] Embodiments provide analyte detection systems and methods for detecting the presence or absence one or more analytes (e.g., mercury, silver, or nucleic acids) in one or more samples. An exemplary detection system includes at least one channel for accommodating a sample and a sensor compound (e.g., TPET2 for mercury detection, TPEA2 for silver detection, or a nucleic acid probe for nucleic acid detection), the channel having a width and a length that is significantly greater in dimension than the width. An exemplary detection system includes an analyte detection circuit programmed or configured

to detect one or more electrical properties along at least a portion of the length of the channel to determine whether the channel contains an analyte of interest.

[0067] In some cases, the sensor compound may be selected such that direct or indirect interaction between particles of the analyte (if present in the sample) and particles of the sensor compound results in formation of an aggregate that alters one or more electrical properties of the channel. In certain cases, an exemplary channel may be configured to have a depth and/or a width that is substantially equal to or smaller than the diameter of a particle of the aggregate formed in the channel due to interaction between particles or ions of an analyte of interest and particles of a sensor compound used to detect the analyte of interest. As such, formation of the aggregate may cause a partial or complete blockage in the flow of conductive particles in the channel, thereby decreasing the electrical current and electrical conductivity along the length of the channel and increasing the resistivity along the length of the channel. An analyte detection circuit may compare this measurable change in the electrical properties of the channel upon introduction of both the sample and the sensor compound, relative to a reference value, to determine if the aggregate is present in the channel. Based on a determination that the aggregate is present in the channel, the analyte detection circuit may determine that the sample contains the analyte of interest.

[0068] In certain other cases, the aggregate particles may be electrically conductive, and formation of the aggregate particles may enhance an electrical pathway along at least a portion of the length of the channel, thereby causing a measurable increase in the electrical conductivity and electrical current measured along the length of the channel. In these cases, formation of the aggregate may cause a measurable decrease in the resistivity along the length of the channel. An analyte detection circuit may compare this measurable change in the electrical properties of the channel upon introduction of both the sample and the sensor compound, relative to a reference value, to determine if the aggregate is present in the channel. Based on a determination that the aggregate is present in the channel, the analyte detection circuit may determine that the sample contains the analyte of interest (e.g., mercury, silver, or nucleic acid).

[0069] Another exemplary technique for detecting analytes (e.g., mercury, silver, or a nucleic acid) may involve detection of the presence of a diode-like behavior in the channel that is caused by the formation of an aggregate in the channel. In the absence of an

aggregate, application of a potential difference having a substantially similar magnitude (e.g., +500 V) may result in a substantially same magnitude of an electrical property (e.g., current) detected along the length of the channel regardless of the direction of application of the potential difference or electric field. If the potential difference is applied across the length of the channel in a first direction along the length of the channel (e.g., such that the positive electrode is at an input port at or near a first end of the channel and such that the negative electrode is at an output port at or near a second end of the channel), the resulting current may be substantially equal in magnitude to the resultant current if the potential difference is applied in the opposite direction (e.g., such that the positive electrode is at the output port and such that the negative electrode is at the input port).

[0070] Formation of an aggregate in the channel may cause a diode-like behavior in which reversal of the direction of the applied potential difference or electric field causes a change in the electrical property detected in the channel. The diode-like behavior causes the detected electrical current to vary in magnitude with the direction of the electric field. When the electric field or potential difference is applied in the first direction, the magnitude of the electrical current may be different in magnitude than when the potential different or electric field is applied in the opposite direction. Thus, comparison between a first electrical property value (detected when a potential difference is applied in a first direction along the channel length) and a second electrical property value (detected when a potential difference is applied in a second opposite direction along the channel length) may enable detection of an aggregate, and thereby detection of the analyte (e.g., mercury, silver, or nucleic acid) in the sample. If the first and second electrical property values are substantially equal in magnitude, then it may be determined that the sample does not contain the analyte (e.g., mercury, silver, or nucleic acid). On the other hand, if the first and second electrical property values are substantially unequal in magnitude, then it may be determined that the sample contains the analyte (e.g., mercury, silver, or nucleic acid). In other words, the sum of the values of the electrical property (positive in one direction, negative in the other direction) is substantially zero in the absence of an aggregate and substantially non-zero in the presence of an aggregate.

[0071] In contrast to conventional nanopore techniques, exemplary embodiments involve detecting one or more electrical properties along the length of the channel, and not

across the depth or thickness dimension of the channel. The channel of exemplary embodiments has a length that is significantly greater in dimension that its width and is not configured as an aperture, hole or pore. The exemplary channel thereby allows a sample and a sensor compound to flow along the length of the channel before the electrical properties are detected, thereby enabling improved dimensional precision and control over the electrical properties. Furthermore, exemplary embodiments are not limited to detection of nucleotides as in conventional nanopore techniques.

[0072] In certain embodiments, one or more properties of the channel other than electrical properties may be detected in determining whether an analyte (e.g., mercury, silver, or a nucleic acid and/or a nucleotide of interest) is present in the channel. These properties may be detected using techniques that include, but are not limited to, acoustic detection, resonance-wise parametric detection, optical detection, spectroscopic detection, fluorescent dyes, and the like.

I. Definition of terms

[0073] Certain terms used in connection with exemplary embodiments are defined below.

[0074] As used herein, the terms "detection system," "detection method" and "detection technique" encompass systems and methods for detecting an analyte in a sample by measuring one or more electrical properties along at least a portion of a length of at least one channel. The analyte may be mercury, silver, or a nucleic acid and/or a nucleotide of interest.

[0075] As used herein, the term "channel" encompasses a conduit in a detection system that is configured to have a well-defined inner surface and an inner space bounded by the inner surface that is configured to accommodate a fluid. In some embodiments, the inner surface of the channel is micro-fabricated and configured to present a smooth surface. An exemplary channel may have the following dimensions: a length, l, measured along its longest dimension (y-axis) and extending along a plane substantially parallel to a substrate of the detection system; a width, w, measured along an axis (x-axis) perpendicular to its longest dimension and extending substantially along the plane parallel to the substrate; and a depth, d, measured along an axis (z-axis) substantially perpendicular to the plane parallel to the

substrate. An exemplary channel may have a length that is substantially greater than its width and its depth. In some cases, exemplary ratios between the length:width may include, but are not limited to, 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 11:1, 12:1, 13:1, 14:1, 15:1, 16:1, 17:1, 18:1, 19:1, 20:1, all intermediate ratios, and the like. In certain cases, an exemplary channel may be configured to have a depth and/or a width that is substantially equal to or smaller than the diameter of an aggregate particle that may be formed in the channel due to interaction between a sensor compound and an analyte of interest.

[0076] As used herein, the term "analyte" encompasses a substance whose presence or absence may be detected using an exemplary detection system or method. Exemplary analytes that may be detected using exemplary embodiments may include organic (e.g., biomolecules) or inorganic (e.g., metal ions) substances. Certain analytes that may be detected using exemplary embodiments include, but are not limited to, silver, mercury, one or more solvents, one or more nucleic acids, and/or one or more nucleotides.

[0077] As used herein, the term "sample" encompasses a test substance that may be analyzed by an exemplary detection system or method to determine whether the sample includes an analyte of interest. Exemplary samples that may be tested in exemplary embodiments include, but are not limited to: any fluids, including those derived from biological fluids like saliva, blood, plasma, urine, stool; soil samples; municipal water samples; air samples; and the like.

[0078] As used herein, the terms "sensor" and "sensor compound" encompass a substance that interacts, directly or indirectly via one or more other sensor compounds, with an analyte of interest in a sample to cause formation of an aggregate. In an example in which an analyte of interest is mercury, a suitable sensor compound may be TPET2. In an example in which an analyte of interest is silver, a suitable sensor compound may be TPEA2. In an example in which an analyte of interest is a nucleic acid and/or a nucleotide, a suitable sensor compound may be one or more nucleic acid probes (e.g., one or more nucleic acid capture probes, one or more nucleic acid cross-linking probes, one or more nucleic acid pre-amplification probes, one or more nucleic acid label extenders, one or more nucleic acid amplification probes, and the like).

[0079] As used herein, the term "aggregate" encompasses a macromolecular structure composed of particles of an analyte and particles of one or more sensor compounds.

As such, an aggregate particle has a unit dimension or unit size that is larger than the unit dimension or unit size of an analyte particle and that is larger than the dimension or unit size of a sensor compound. An aggregate may form in a channel of an exemplary detection system due to direct and/or indirect interaction between the particles of an analyte and the particles of one or more sensor compounds. In exemplary detection systems and methods for detecting a particular analyte, one or more sensor compounds may be selected such that the sensor compounds interact with the analyte, directly or indirectly via other substances, to result in formation of an aggregate in a channel. Presence of the aggregate particles in the channel therefore indicates presence of the analyte in the channel, whereas absence of the aggregate particles in the channel indicates absence of the analyte in the channel.

[0080] In certain cases in which a potential difference is applied across at least a portion of the length of the channel, formation of an aggregate may cause a partial or complete blockage in fluid flow in the channel and may cause a measurable decrease in an electrical conductivity or current along at least a portion of the length of the channel and/or a measurable increase in the electrical resistivity. In certain other cases, particles of an aggregate may be electrically conductive, and therefore formation of the aggregate may enhance the electrical conductivity of the channel, thereby causing a measurable increase in the electrical conductivity or current along at least a portion of the length of the channel and/or a measurable decrease in the electrical resistivity.

[0081] As used herein, the term "electrical property" encompasses one or more characteristics of a channel including, but not limited to, measures that quantify how much electric current is conducted along the channel, the ability of the channel (and/or any contents of the channel) to conduct an electric current, how strongly the channel (and/or any contents of the channel) opposes the flow of electrical current, and the like. In exemplary embodiments, an electrical property may be detected along at least a portion of the length of the channel. Exemplary electrical properties detected in embodiments include, but are not limited to, a measure of an electrical current conducted along at least a portion of the length of the channel, a measure of an electrical conductivity along at least a portion of the length of the channel, a measure of electrical resistivity along at least a portion of the length of the channel, a measure of potential difference across at least a portion of the length of a channel, combinations thereof, and the like.

[0082] As used herein, the term "reference" with respect to an electrical property value encompasses a value or range of values of an electrical property of a channel prior to a state in which both a sample and all necessary sensor compounds (e.g., TPET2, TPEA2, or nucleic acid probes) have been introduced into the channel and allowed to interact with each other in the channel. That is, the reference value is a value characterizing the channel prior to interaction between an analyte of interest in the sample and all of the sensor compounds used to detect the analyte of interest. In some cases, the reference value may be detected at a time period after introduction of one or more sensor compounds into the channel but before introduction of a sample into the channel. In some cases, the reference value may be detected at a time period after introduction of the sample into the channel but before introduction of all of the sensor compounds into the channel (e.g., before introduction of at least one sensor compound into the channel). In some cases, the reference value may be detected at a time period before introduction of either the sample or the sensor compounds into the channel. In some cases, the reference value may be detected at a time period before introduction of either the sample or the sensor compounds into the channel but after introduction of a buffer solution into the channel.

[0083] In some cases, the reference value may be predetermined and stored on a non-transitory storage medium from which it may be accessed. In other cases, the reference value may be determined from one or more electrical property measurements during use of the detection system.

[0084] As used herein, the terms "data," "content," "information," and similar terms may be used interchangeably to refer to data capable of being transmitted, received, and/or stored in accordance with embodiments of the present invention. Thus, use of any such terms should not be taken to limit the spirit and scope of embodiments of the present invention. Further, where a module, processor or device is described herein to receive data from another module, processor or device, it will be appreciated that the data may be received directly from the another module, processor or device or may be received indirectly via one or more intermediary modules or devices, such as, for example, one or more servers, relays, routers, network access points, base stations, hosts, and/or the like, sometimes referred to herein as a "network." Similarly, where a computing device is described herein to send data to another computing device, it will be appreciated that the data may be sent

directly to the another computing device or may be sent indirectly via one or more intermediary computing devices, such as, for example, one or more servers, relays, routers, network access points, base stations, hosts, and/or the like.

[0085] As used herein, the term "module," encompasses hardware, software and/or firmware configured to perform one or more particular functions.

[0086] As used herein, the term "computer-readable medium" refers to a non-transitory storage hardware, non-transitory storage device or non-transitory computer system memory that may be accessed by a controller, a microcontroller, a computational system or a module of a computational system to encode thereon computer-executable instructions or software programs. A "non-transitory computer-readable medium" may be accessed by a computational system or a module of a computational system to retrieve and/or execute the computer-executable instructions or software programs encoded on the medium. A non-transitory computer-readable medium may include, but is not limited to, one or more types of non-transitory hardware memory, non-transitory tangible media (for example, one or more magnetic storage disks, one or more optical disks, one or more USB flash drives), computer system memory or random access memory (such as, DRAM, SRAM, EDO RAM), and the like.

[0087] As used herein, the term "set" refers to a collection of one or more items.

[0088] As used herein, the term "plurality" refers to two or more items.

[0089] As used herein, the terms "equal" and "substantially equal" refer interchangeably, in a broad lay sense, to exact equality or approximate equality within some tolerance.

[0090] As used herein, the terms "similar" and "substantially similar" refer interchangeably, in a broad lay sense, to exact sameness or approximate similarity within some tolerance.

[0091] As used herein, the terms "couple" and "connect" encompass direct or indirect connection among two or more components. For example, a first component may be coupled to a second component directly or through one or more intermediate components.

[0091a] The term "comprising" as used in this specification and claims means "consisting at least in part of". When interpreting statements in this specification and claims which include the term "comprising", other features besides the features prefaced by this

term in each statement can also be present. Related terms such as "comprise" and "comprises" are to be interpreted in similar manner.

[0092] Some exemplary embodiments of the present invention will now be described more fully hereinafter with reference to the accompanying drawings in which some, but not all, embodiments of the inventions are shown. Indeed, these inventions may be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure will satisfy applicable legal requirements. Like numbers refer to like elements throughout.

II. Exemplary analyte detection systems

[0093] An exemplary detection system includes at least one channel, and detects one or more electrical properties along at least a portion of the length of the channel to determine whether the channel contains an analyte (e.g., mercury; silver; or a particular nucleic acid of interest and/or a particular nucleotide of interest). An exemplary detection system may be configured to include one or more channels for accommodating a sample and one or more sensor compounds (e.g., TPET2 for mercury detection, TPEA2 for silver detection, or one or more nucleic acid probes for nucleic acid detection), one or more input ports for introduction of the sample and the sensor compounds into the channel and, in some embodiments, one or more output ports through which the contents of the channel may be removed.

[0094] One or more sensor compounds may be selected such that direct or indirect interaction between particles of the analyte, if present in the sample, and particles of the sensor compound result in formation of an aggregate that alters one or more electrical properties of at least a portion of the length of the channel. In certain cases, formation of the aggregate particles may inhibit or block fluid flow in the channel, and may therefore cause a measurable drop in the electrical conductivity and electrical current measured along the length of the channel. Similarly, in these cases, formation of the aggregate may cause a measurable increase in the resistivity along the length of the channel. In certain other cases, the aggregate particles may be electrically conductive, and formation of the aggregate particles may enhance an electrical pathway along at least a portion of the length of the channel, thereby causing a measurable increase in the electrical conductivity and electrical

current measured along the length of the channel. In these cases, formation of the aggregate may cause a measurable decrease in the resistivity along the length of the channel.

[0095] An exemplary channel may have the following dimensions: a length measured along its longest dimension (y-axis) and extending along a plane parallel to the substrate of the detection system; a width measured along an axis (x-axis) perpendicular to its longest dimension and extending along the plane parallel to the substrate; and a depth measured along an axis (z-axis) perpendicular to the plane parallel to the substrate. An exemplary channel may have a length that is substantially greater than its width and its depth. In some cases, exemplary ratios between the length:width may be 2:1, 3:1, 4:1, 5:1, 6:1, 7:1, 8:1, 9:1, 10:1, 11:1, 12:1, 13:1, 14:1, 15:1, 16:1, 17:1, 18:1, 19:1, 20:1, intermediate ratios, and the like.

[0096] In certain cases, an exemplary channel may be configured to have a depth and/or a width that is substantially equal to or smaller than the diameter of a particle of an aggregate formed in the channel due to interaction between particles of an analyte of interest (e.g., mercury, silver, or a nucleic acid) and particles of a sensor compound (e.g., TPET2 for mercury detection, TPEA2 for silver detection, or a nucleic acid probe for nucleic acid detection) used to detect the analyte.

[0097] An exemplary channel may have a width taken along the x-axis ranging from 1 nm to 50,000 nm, but is not limited to this exemplary range. An exemplary channel may have a length taken along the y-axis ranging from 10 nm to 2 cm, but is not limited to this exemplary range. An exemplary channel may have a depth taken along the z-axis ranging from 1 nm to 1 micron, but is not limited to this exemplary range.

[0098] An exemplary channel may have any suitable transverse cross-sectional shape (e.g., a cross-section taken along the x-z plane) including, but not limited to, circular, elliptical, rectangular, square, D-shaped (due to isotropic etching), and the like.

[0099] Figures 1A and 1B illustrate an exemplary detection system 100 that may be used to detect presence or absence of an analyte (e.g., mercury; silver; or a particular nucleic acid or particular nucleotide) in a sample. Figure 1A is a top view of the system, while Figure 1B is a cross-sectional side view of the system. The detection system 100 includes a substrate 102 that extends substantially along a horizontal x-y plane. In some embodiments, the substrate 102 may be formed of a dielectric material, for example, silica.

Other exemplary materials for the substrate 102 include, but are not limited to, glass, sapphire, diamond, and the like.

[0100] The substrate 102 may support or include a channel 104 having at least an inner surface 106 and an inner space 108 for accommodating a fluid. In some cases, the channel 104 may be etched in a top surface of the substrate 102. Exemplary materials for the inner surfaces 106 of the channel 104 include, but are not limited to, glass, silica, and the like.

[0101] The channel 104 and the substrate 102 may be formed of glass in certain embodiments. Biological conditions represent a barrier to the use of glass-derived implantations due to the slow dissolution of glass into biological fluids and adhesion of proteins and small molecules to the glass surface. In certain non-limiting embodiments, surface modification using a self-assembled monolayer offers an approach for modifying glass surfaces for analyte detection and analysis. In certain embodiments, at least a portion of the inner surface 106 of the channel 104 may be pre-treated or covalently modified to include or be coated with a material that enables specific covalent binding of a sensor compound to the inner surface. In certain embodiments, a cover slip 114 covering the channel may also be covalently modified with a material.

[0102] Exemplary materials that may be used to modify the inner surface 106 of the channel 104 include, but are not limited to, a silane compound (e.g., tricholorsilane, alkylsilane, triethoxysilane, perfluoro silane), zwitterionic sultone, poly(6-9)ethylene glycol (Peg), perfluorooctyl, fluorescein, an aldehyde, a graphene compound, and the like. The covalent modification of the inner surface of the channel may prevent non-specific absorption of certain molecules. In one example, covalent modification of the inner surface may enable covalent bonding of sensor compound molecules to the inner surface while preventing non-specific absorption of other molecules to the inner surface. For example, poly(ethylene glycol) (Peg) may be used to modify the inner surface 106 of the channel 104 to reduce non-specific adsorption of materials to the inner surface.

[0103] In some embodiments, the channel 104 may be nano or micro-fabricated to have a well-defined and smooth inner surface 106. Exemplary techniques for fabricating a channel and modifying the inner surface of a channel are taught in Sumita Pennathur and Pete Crisalli (2014), "Low Temperature Fabrication and Surface Modification Methods for

Fused Silica Micro- and Nanochannels", MRS Proceedings, 1659, pp 15-26. doi:10.1557/opl.2014.32, the entire contents of which are expressly incorporated herein by reference.

[0104] A first end section of the channel 104 may include or be in fluid communication with an input port 110, and a second end section of the channel 104 may include or be in fluid communication with an output port 112. In certain non-limiting embodiments, the ports 110 and 112 may be provided at terminal ends of the channel 104.

[0105] The top surface of the substrate 102 having the channel 104 and the ports 110, 112 may be covered and sealed with a cover slip 114 in some embodiments.

[0106] A first electrode 116 may be electrically connected at the first end section of the channel 104, for example, at or near the input port 110. A second electrode 118 may be electrically connected at the second end section of the channel 104, for example, at or near the output port 112. The first and second electrodes 116, 118 may be electrically connected to a power supply or voltage source 120 in order to apply a potential difference between the first and second electrodes. That is, the potential difference is applied across at least a portion of the length of the channel. When a fluid is present in the channel 104 and is under the influence of the applied potential difference, the electrodes 116, 118 and the fluid may create a complete electrical pathway.

[0107] The power supply or voltage source 120 may be configured to apply an electric field in a reversible manner such that a potential difference is applied in a first direction along the channel length (along the y-axis) and also in a second opposite direction (along the y-axis). In one example in which the electric field or potential difference direction is in a first direction, the positive electrode may be connected at the first end section of the channel 104, for example, at or near the input port 110, and the negative electrode may be connected at the second end section of the channel 104, for example, at or near the output port 112. In another example in which the electric field or potential difference direction is in a second opposite direction, the negative electrode may be connected at the first end section of the channel 104, for example, at or near the input port 110, and the positive electrode may be connected at the second end section of the channel 104, for example, at or near the output port 112.

[0108] The first and second end sections of the channel 104 (e.g., at or near the input port 110 and the output port 112) may be electrically connected to the analyte detection circuit 122 that is programmed or configured to detect values of one or more electrical properties of the channel 104 for determining whether an analyte is present or absent in the channel 104. The electrical property values may be detected at a single time period (for example, a certain time period after introduction of a sample and one or more sensor compounds into the channel), or at multiple different time periods (for example, before and after introduction of both the sample and one or more sensor compound into the channel). Exemplary electrical properties detected may include, but are not limited to, electrical current, conductivity voltage, resistance, and the like. Certain exemplary analyte detection circuits 122 may include or be configured as a processor or a computing device, for example as device 1700 illustrated in Figure 18. Certain other analyte detection circuits 122 may include, but are not limited to, an ammeter, a voltmeter, an ohmmeter, and the like.

[0109] In one embodiment, the analyte detection circuit 122 may include a measurement circuit 123 programmed or configured to measure one or more electrical property values along at least a portion of a length of the channel 104. The analyte detection circuit 122 may also include an equilibration circuit 124 that is programmed or configured to periodically or continually monitor one or more values of an electrical property of the channel over a time period, and to select a single one of the values after the values have reached equilibrium (i.e., have stopped varying beyond a certain threshold of variance or tolerance).

[0110] The analyte detection circuit 122 may also include a comparison circuit 126 that is programmed or configured to compare two or more electrical property values of the channel, for example, a reference electrical property value (measured before a state in which both the sample and all of the sensor compounds have been introduced into the channel) and an electrical property value (measured after introduction of the sample and all of the sensor compound into the channel). The comparison circuit 126 may use the comparison in order to determine whether an analyte of interest is present or absent in the channel. In one embodiment, the comparison circuit 126 may calculate a difference between the measured electrical property value and the reference electrical property value, and

compare the difference to a predetermined value indicative of the presence or absence of the analyte in the channel.

[0111] In certain embodiments, upon introduction of both the sample and the sensor compound into the channel, the comparison circuit 126 may be programmed or configured to compare a first electrical property value (e.g., magnitude of electrical current) when the electric field or potential difference is applied across the channel in a first direction along the length of the channel to a second electrical property value (e.g., magnitude of electrical current) when the electric field or potential difference is applied across the channel in a second opposite direction along the length of the channel. In one embodiment, the comparison circuit 126 may calculate a difference between the magnitudes of the first and second values, and compare the difference to a predetermined value (e.g., whether the difference is substantially zero) indicative of the presence or absence of the analyte in the channel. For example, if the difference is substantially zero, this indicates absence of the analyte aggregate in the channel, e.g., absence of the analyte in the channel. If the difference is substantially non-zero, this indicates presence of the analyte aggregate in the channel, e.g., presence of the analyte in the channel.

[0112] In certain embodiments, the analyte detection circuit 122 may be programmed or configured to determine an absolute concentration of an analyte in a sample, and/or a relative concentration of an analyte relative to one or more additional substances in a sample.

[0113] In some embodiments, the comparison circuit 124 and the equilibration circuit 126 may be configured as separate circuits or modules; while in other embodiments, they may be configured as a single integrated circuit or module.

[0114] The analyte detection circuit 122 may have an output 128 that may, in some embodiments, be connected to one or more external devices or modules. For example, the analyte detection circuit 122 may transmit a reference electrical property value and/or one or more measured electrical property values to one or more of: a processor 130 for further computation, processing and analysis, a non-transitory storage device or memory 132 for storage of the values, and a visual display device 134 for display of the values to a user. In some cases, the analyte detection circuit 122 may itself generate an indication of whether the

sample includes the analyte, and may transmit this indication to the processor 130, the non-transitory storage device or memory 132 and/or the visual display device 134.

[0115] In an exemplary method of using the system of Figures 1A and 1B, one or more sensor compounds, and a sample may be sequentially or concurrently introduced into the channel.

[0116] When flow of the fluid and/or flow of the charged particles in the fluid is uninhibited (for example, due to absence of an aggregate), the conductive particles or ions in the fluid may travel along at least a portion of the length of the channel 104 along the y-axis from the input port 110 toward the output port 112. The movement of the conductive particles or ions may result in a first or "reference" electrical property value or range of values (e.g., of an electrical current, conductivity, resistivity) being detected by the analyte detection circuit 122 along at least a portion of the length of the channel 104. In some embodiments, the equilibration circuit 124 may periodically or continually monitor electrical property values during a time period until the values reach equilibrium. The equilibration circuit 124 may then select one of the values as the reference electrical property value to avoid the influence of transient changes in the electrical property.

[0117] The term "reference" electrical property value may refer to a value or range of values of an electrical property of a channel prior to introduction of a sample and all of the sensor compounds (e.g., TPET2 for mercury detection, TPEA2 for silver detection, or one or more nucleic acid probes) into the channel. That is, the reference value is a value characterizing the channel prior to any interaction between analytes in the sample and all of the sensor compounds. In some cases, the reference value may be detected at a time period after introduction of a sensor compound into the channel but before introduction of the sample and additional sensor compounds into the channel. In some cases, the reference value may be detected at a time period after introduction of a sensor compound and the sample into the channel but before introduction of additional sensor compounds into the channel. In some cases, the reference value may be detected at a time period before introduction of the sample or the sensor compounds into the channel. In some cases, the reference value may be predetermined and stored on a non-transitory storage medium from which it may be accessed.

[0118] In some cases, formation of an electrically conductive aggregate in the channel (due to interactions between an analyte of interest in the sample and one or more sensor compounds) may enhance the electrical pathway along at least a portion of the length of the channel 104. In this case, the detection circuit 122 may detect a second electrical property value or range of values (e.g., of an electrical current, conductivity, resistivity) along at least a portion of the length of the channel 104. In some embodiments, the detection circuit 122 may wait for a waiting or adjustment time period after introduction of the sample and all of the sensor compounds into the channel prior to detecting the second electrical property value. The waiting or adjustment time period allows an aggregate to form in the channel and for the aggregate formation to alter the electrical properties of the channel.

[0119] In some embodiments, the equilibration circuit 124 may periodically or continually monitor electrical property values during a time period after the introduction of the sample and the sensor compound until the values reach equilibrium. The equilibration circuit 124 may then select one of the values as the second electrical property value to avoid the influence of transient changes in the electrical property.

[0120] The comparison circuit 126 may compare the second electrical property value to the reference electrical property value. If it is determined that the difference between the second value and the reference value corresponds to a predetermined range of increase in current or conductivity (or decrease in resistivity), the detection circuit 122 may determine that an aggregate is present in the channel and that, therefore, the analyte is present in the sample.

[0121] In certain other cases, when flow of the fluid in the channel and/or flow of the charged particles in the fluid is partially or completely blocked (for example, by formation of an aggregate), the conductive particles or ions in the fluid may be unable to freely travel along at least a portion of the length of the channel 104 along the y-axis from the input port 110 toward the output port 112. The hindered or stopped movement of the conductive particles or ions may result in a third electrical property value or range of values (e.g., of an electrical current, conductivity, resistivity) being detected by the analyte detection circuit 122 along at least a portion of the length of the channel 104. The third electrical property value may be detected in addition to or instead of the second electrical property value. In some embodiments, the analyte detection circuit 122 may wait for a waiting or

adjustment time period after introduction of both the sample and the sensor compound into the channel prior to detecting the third electrical property value. The waiting or adjustment time period allows an aggregate to form in the channel and for the aggregate formation to alter the electrical properties of the channel.

[0122] In some embodiments, the equilibration circuit 124 may periodically or continually monitor electrical property values during a time period after the introduction of the sample and the sensor compound until the values reach equilibrium. The equilibration circuit 124 may then select one of the values as the third electrical property value to avoid the influence of transient changes in the electrical property.

[0123] The comparison circuit 126 may compare the third electrical property value to the reference electrical property value. If it is determined that the difference between the third value and the reference value corresponds to a predetermined range of decrease in current or conductivity (or increase in resistivity), the analyte detection circuit 122 may determine that an analyte aggregate is present in the channel and that, therefore, the analyte of interest is present in the sample.

[0124] The fluid flow along the length of the channel may depend on the size of the aggregate particles in relation to the dimensions of the channel, and the formation of an electrical double layer (EDL) at the inner surface of the channel. Figure 2 illustrates a cross-sectional side view of an exemplary channel of the detection system of Figures 1A and 1B, in which the combination of an electric double layer (EDL) 202 at the inner surface of the channel and aggregate particles 204 is shown to inhibit fluid flow in the channel.

[0125] In general terms, an EDL is a region of net charge between a charged solid (e.g., the inner surface of the channel, an analyte particle, an aggregate particle) and an electrolyte-containing solution (e.g., the fluid contents of the channel). EDLs exist around both the inner surface of the channel and around any analyte particles and aggregate particles within the channel. The counter-ions from the electrolyte are attracted towards the charge of the inner surface of the channel, and induce a region of net charge. The EDL affects ion flow within the channel and around analyte particles and aggregate particles of interest, creating a diode-like behavior by not allowing any of the counter-ions to pass through the length of the channel.

[0126] To mathematically solve for the characteristic length of the EDL, the Poisson-Boltzmann (PB) equation and/or Poisson-Nernst-Plank equations (PNP) may be solved. These solutions are coupled to the Navier-Stokes (NS) equations for fluid flow to create a nonlinear set of coupled equations that are analyzed to understand the operation of the exemplary system.

[0127] In view of the dimensional interplay among the channel surface, the EDLs and the aggregate particles, exemplary channels may be configured and constructed with carefully selected dimensional parameters that ensure that flow of conductive ions is substantially inhibited along the length of the channel when an aggregate of a certain predetermined size is formed in the channel. In certain cases, an exemplary channel may be configured to have a depth and/or a width that is substantially equal to or smaller than the diameter of an aggregate particle formed in the channel during analyte detection. In certain embodiments, the sizes of the EDLs may also be taken into account in selecting dimensional parameters for the channel. In certain cases, an exemplary channel may be configured to have a depth and/or a width that is substantially equal to or smaller than the dimension of the EDL generated around the inner surface of the channel and the aggregate particles in the channel.

[0128] In certain embodiments, prior to use of the detection system, the channel may be free of the sensor compound (e.g., TPET2 for mercury detection, TPEA2 for silver detection, or one or more nucleic acid probes for nucleic acid detection). That is, a manufacturer of the detection system may not pre-treat or modify the channel to include the sensor compound. In this case, during use, a user may introduce one or more sensor compounds, for example in an electrolyte buffer, into the channel and detect a reference electrical property value of the channel with the sensor compound but in the absence of a sample.

[0129] In certain other embodiments, prior to use of the detection system, the channel may be pre-treated or modified so that at least a portion of an inner surface of the channel includes or is coated with a sensor compound (e.g., TPET2 for mercury detection, TPEA2 for silver detection, or one or more nucleic acid probes for nucleic acid detection). That is, a manufacturer of the detection system may pre-treat or modify the channel to include the sensor compound. In this case, a user may only need to introduce the sample into the channel. In one example, the manufacturer may detect a reference electrical property

value of the channel modified with the sensor compound and, during use, a user may use the stored reference electrical property value. That is, a manufacturer of the detection system may pre-treat or modify the channel to include a sensor compound. In this case, a user may need to introduce the sample and one or more additional sensor compounds into the channel.

[0130] Certain exemplary detection systems may include a single channel. Certain other exemplary detection systems may include multiple channels provided on a single substrate. Such detection systems may include any suitable number of channels including, but not limited to, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 channels.

[0131] In one embodiment, a detection system may include a plurality of channels in which at least two channels operate independent of each other. The exemplary channel 104 and associated components of Figures 1A and 1B may be reproduced on the same substrate to achieve such a multi-channel detection system. The multiple channels may be used to detect the same analyte in the same sample, different analytes in the same sample, the same analyte in different samples, and/or different analytes in different samples.

[0132] In another embodiment, a detection system may include a plurality of channels in which at least two channels operate in cooperation with each other. Figure 3 illustrates an exemplary detection system 300 including a substrate 302. The substrate 302 may include a plurality of channels 304, 306 that may be used to detect the same analyte in the same sample. Although two channels are represented, more channels may be provided in the detection system. The provision of multiple channels may allow redundancy and error-checking functionalities, whereby different analyte (detection results in the channels may indicate that the detection system is not performing reliably and whereby the same result in the channels may indicate that the detection system is performing reliably. In the former case, the detection system may need to be repaired, recalibrated or discarded.

[0133] First end sections of the first channel 304 and the second channel 306 may include or be in fluid communication with a common input port 308 at which a sample and one or more sensor compounds may be introduced into the detection system. A second end section of the first channel 304 may include or be in fluid communication with a first output port 310, and a second end section of the second channel 306 may include or be in fluid

communication with a second output port 312. The output ports 310 and 312 may not be in fluid communication with each other.

[0134] The detection system 300 may include electrodes 314, 316A and 316B that may be electrically connected at or near the end sections of the first and second channels 304, 306. The electrodes 314, 316A and 316B may connect the channels 304, 306 to a voltage or power supply 332 in order to apply a potential difference across the input port 308 and the first output port 310 and across the input port 308 and the second output port 312. Similarly, the analyte detection circuit 318 may be electrically connected at or near the end sections of the first and second channels 304, 306 to determine whether the sample introduced into both channels contain an analyte of interest.

[0135] Components represented in Figure 3 that are in common with components represented in Figures 1A and 1B are described in connection with Figures 1A and 1B.

[0136] In another embodiment, a detection system may include a plurality of channels in which at least two channels operate in cooperation with each other. Figure 4 illustrates an exemplary detection system 400 including a substrate 402. The substrate 402 may include a plurality of channels 404, 406 that may be used to detect the same analyte in different samples or different analytes in the same sample. Although two channels are represented, more channels may be provided in the detection system. The provision of multiple channels may allow concurrent detection of multiple analytes in the same sample or the same analyte in multiple samples, thereby improving the speed and throughput of the detection system.

[0137] First end sections of the first channel 404 and the second channel 406 may include or be in fluid communication with a common first input port 408 at which a sample or one or more sensor compounds may be introduced into the detection system. In addition, the first end section of the first channel 404 may include or be in fluid communication with a second input port 414. The first end section of the second channel 406 may include or be in fluid communication with a third input port 416. The second and third input ports 414, 416 may not be in fluid communication with other.

[0138] A second end section of the first channel 404 may include or be in fluid communication with a first output port 410, and a second end section of the second channel

406 may include or be in fluid communication with a second output port 412. The output ports 410 and 412 may not be in fluid communication with each other.

[0139] The detection system 400 may include electrodes 418, 420 and 422 that may be electrically connected at or near the end sections of the first and second channels 404, 406. The electrodes may electrically connect the first and second channels to a voltage or power source 436 in order to apply a potential difference across the first input port 408 and the first output port 410 and across the first input port 408 and the second output port 412. Similarly the analyte detection circuit 424 may be electrically connected at or near the end sections of the first and second channels 404, 406 to determine whether one or more samples introduced into the channels contain one or more analytes of interest.

[0140] Components represented in Figure 4 that are in common with components represented in Figures 1A and 1B are described in connection with Figures 1A and 1B.

[0141] In an exemplary method of using the system 400 of Figure 4, a sample may be introduced into the common first input port 408, and first and second sets of sensor compounds may be introduced at the second and third input ports 414 and 416, respectively. As a result, based on measurements taken at the first and second end sections of the first channel 404, the analyte detection circuit 424 may determine whether the sample includes a first analyte of interest (which interacts with the first sensor compound in the first channel to form an aggregate). Based on measurements taken at the first and second end sections of the second channel 406, the analyte detection circuit 424 may determine whether the sample includes a second analyte of interest (which interacts with the second sensor compound in the second channel to form an aggregate).

[0142] In another exemplary method of use, one or more sensor compounds may be introduced into the common first input port 408, and first and second samples may be introduced at the second and third input ports 414 and 416, respectively. As a result, based on measurements taken at the first and second end sections of the first channel 404, the analyte detection circuit 424 may determine whether the first sample includes an analyte of interest which interacts with the sensor compound in the first channel to form an aggregate). Based on measurements taken at the first and second end sections of the second channel 406, the analyte detection circuit may 424 determine whether the second sample includes the same

analyte of interest (which interacts with the sensor compound in the second channel to form an aggregate).

[0143] In certain embodiments, the systems illustrated in Figures 1A, 1B, 3 and 4 may be used to determine an absolute or relative concentration of the analyte based on one or more electrical property values of the channel. The concentration of an analyte may be determined in such a manner because the channels of exemplary detection systems have a high inner surface area to volume ratio. At low concentrations of the analyte, electrical conductivity in the channel is dominated by surface charges. As such, measurements of electrical properties of the channel can enable distinction between different ions. As a result, unique and sensitive measurements of the bulk flow in the channel can be used to determine information on the surface charges at the inner surface of the channel. Exemplary embodiments may thus compute predetermined ranges of electrical property values of the channel that are characteristic of a particular analyte given the dimensions of the channel and at different concentrations of the analyte. These predetermined values may then be used to determine an unknown concentration of an analyte in a sample.

[0144] Detailed information on surface charges in the channel for different ions is presented in the following papers, the entire contents of which are expressly incorporated herein by reference: "Surface-dependent chemical equilibrium constants and capacitances for bare and 3-cyanopropyldimethylchlorosilane coated silica nanochannels," M. B. Andersen, J. Frey, S. Pennathur and H. Bruus, J. Colloid Interface Sci. 353, 301-310 (2011), and "Hydronium-domination ion transport in carbon-dioxide-saturated electrolytes at low salt concentrations in nanochannels"," K.L. Jensen, J.T. Kristensen, A.M. Crumrine, M.B.Andersen, H. Bruus and S. Pennathur., Phys. Review E. 83, 5, 056307.

[0145] Figure 5 is a schematic drawing of the inside of a channel including an inner surface of the channel 502, an immobile layer of fluid 504 lying immediately adjacent to the inner surface of the channel, a diffusive layer of fluid 506 lying immediately adjacent to the immobile layer, and a bulk fluid flow layer 508 lying immediately adjacent to the diffusive layer. Exemplary ions are represented in each of the fluid layers. Upon application of a potential difference across the length of the channel, an electrical property value may be detected along at least a portion of the length of the channel (for example, by the analyte detection circuit 122). The comparison circuit 126 may be used to compare the measured

electrical property value to a predetermined range of electrical property values that correspond to a particular concentration or range of concentration values of the analyte. The concentration determined may be an absolute concentration of the analyte or a relative concentration of the analyte with respect to the concentrations of one or more other substances in the channel.

[0146] Figures 6A and 6B are graphs showing conductivity values measured in a channel for different test cases. In each test case, a different relative concentration of an analyte relative to concentrations of two additional substances (in this case, ammonium and hydrogen peroxide) is used, and the corresponding conductivity value is determined in the channel. In one embodiment, Standard Clean 1 or SC1 is used a solution in the test cases. Details of SC1 can be found online. The ratios of concentrations among the three substances in the test cases represented in Figures 6A and 6B are presented in TABLE 1, which lists test case ratios for the concentration of SC1 to the concentration of hydrogen peroxide to the concentration of ammonium.

TABLE 1

Test Case	Water : Hydrogen Peroxide : Ammonium Hydroxide
A	5:1:1
B	4.8:1.3:0.75
C	5.1:0.62:1.3
D	5.26:0.24:1.5
E	4.92:1.3:0.83
F	3500:10:10
G	3501:3.95:14
H	3497:16:06
I	3501:6.97:12
J	3499:12.5:8.3

[0147] The lower the concentration of an analyte, the easier it is to measure differences in relative concentrations between the analyte and other substances. For example, at concentration ratios of 1000:1:1, detection sensitivity on the order of 1-10 ppm may be achieved in the exemplary detection system. At concentration ratios of 350:1:1, detection

sensitivity on the order of 100 ppm may be achieved. At concentration ratios of 5:1:1, detection sensitivity on the order of 10,000 ppm may be achieved.

[0148] The substrate 102, the channel 104 and the cover slip 114 of Figures 1A and 1B may be formed of glass in certain embodiments. Biological conditions represent a barrier to the use of glass-derived implantations due to the slow dissolution of glass into biological fluids and adhesion of proteins and small molecules to the glass surface. In exemplary embodiments, surface modification using a self-assembled monolayer offers an approach for modifying glass surfaces for analyte detection and analysis. In certain embodiments, at least a portion of the inner surface 106 of the channel 104 and/or the inner surface of the cover slip 114 may be pre-treated or covalently modified to include or be coated with a material that enables specific covalent binding of a sensor compound (e.g., TPET2 for mercury detection, or one or more nucleic acid probes for nucleic acid detection) to the inner surface.

[0149] Exemplary materials that may be used to modify the inner surface of the channel and/or the cover slip include, but are not limited to, a silane compound (e.g., tricholorsilane, alkylsilane, triethoxysilane, perfluoro silane), zwitterionic sultone, poly(6-9)ethylene glycol (Peg), perfluorooctyl, fluorescein, an aldehyde, a graphene compound, and the like. The covalent modification of the inner surface of the channel may prevent non-specific absorption of certain molecules. In one example, covalent modification of the inner surface may enable covalent bonding of sensor compound molecules to the inner surface while prevent non-specific absorption of other molecules to the inner surface.

[0150] As one example of a modification material, alkysilanes are a group of molecules that form covalent monolayers on the surfaces of silicon and glass. Alkylsilanes have three distinct regions: a head group surrounded by good leaving groups, a long alkyl chai, and a terminal end group. The head group, usually containing a halogen, alkoxy or other leaving group, allows the molecule to covalently anchor to the solid glass surface under appropriate reaction conditions. The alkyl chain contributes to the stability and ordering of the monolayer through Vander-Waals interactions, which allows for the assembly of a well ordered monolayer. The terminal end group allows for the functionalization and tunability of chemical surface properties by using techniques including, but not limited to, nucleophilic substitution reactions, click chemistry or polymerization reactions.

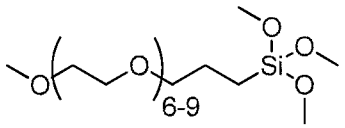
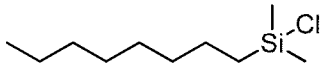
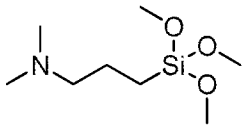
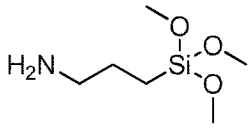
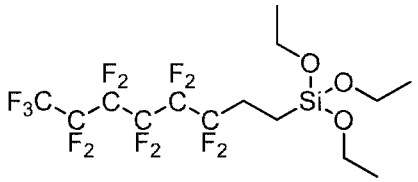
[0151] In one exemplary technique of treating the inner surface with a silane compound, a solution is produced. The solution may be between 0.1% and 4% v/v (if silane is liquid) or w/v (if silane is a solid) of appropriate chloro-, trichloro-, trimethoxy- or triethoxysilane in the appropriate solvent (e.g. toluene for trimethoxy- or triethoxysilanes, ethanol for chloro- or trichlorosilanes or water with a pH between 3.5 to 5.5 for trimethoxysilanes). The solution may be filtered through a 0.2 micron surfactant free cellulose acetate (SFCA) filter. 10 μL of the filtered silane solution may be added to a port of the channel and allowed to capillary fill the channel. This may or may not be observed by light microscopy and may take between five and forty minutes depending upon the solvent composition. After capillary filling is complete, 10 μL of the filtered silane solution may be added to the remaining ports of the channel. The entire channel may then be immersed in the filtered silane solution and allowed to react for a desired amount of time (for example, 1 to 24 hours) at a desired temperature (for example, 20°C to 80°C depending upon the specific silane and solvent composition used for the modification). After the desired reaction time is over, the silanization process may be quenched using one of the following techniques, and catalytic amount of acetic acid may be added to toluene or ethanol-based surface modifications in some cases.

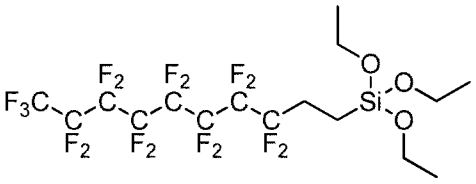
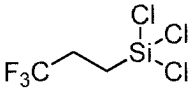
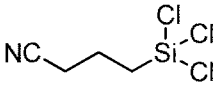
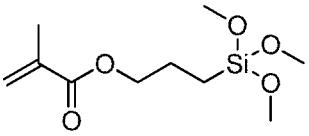
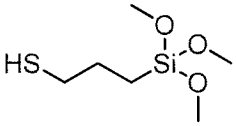
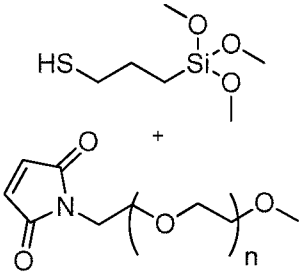
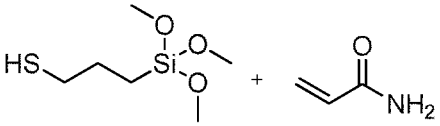
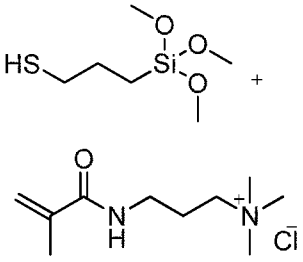
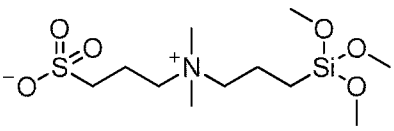
[0152] In one exemplary technique of quenching, the entire channel may be transferred to a container filled with 0.2 micron SFCA filtered ethanol, and stored until the desired time for use or further modification. In another exemplary technique of quenching, the channel may be electrokinetically washed with an appropriate solvent composition. In one electrokinetic washing technique for toluene modification of a channel, toluene is electrokinetically driven through the channel at a 10V to 1000V differential between electrodes for 5 to 15 minutes, followed by electrokinetically driving ethanol through the channel at a 10V to 1000V differential between electrodes for 5 to 15 minutes, followed by electrokinetically driving a 1:1 mixture of ethanol:water through the channel at 10V to 1000V differential between electrodes for 5 to 15 minutes, followed by a final electrokinetic driving of water through the channel at 10V to 1000V for 5 to 15 minutes. Proper operation of the channel may be confirmed by measuring the current at 1000V applied field to an added 50 mM sodium borate buffer in the channel (giving a current reading of approximately 330

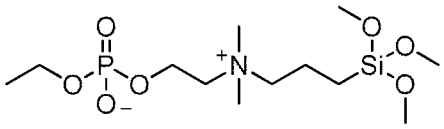
nA based on channel dimensions) and re-addition of ultrapure (e.g., MilliQ ultrapure) water at the same applied field affording a current of less than 20 nA but greater than zero

[0153] TABLE 2 summarizes certain exemplary materials that may be used to modify an inner surface of a channel and/or an inner surface of a cover slip covering the channel.

TABLE 2

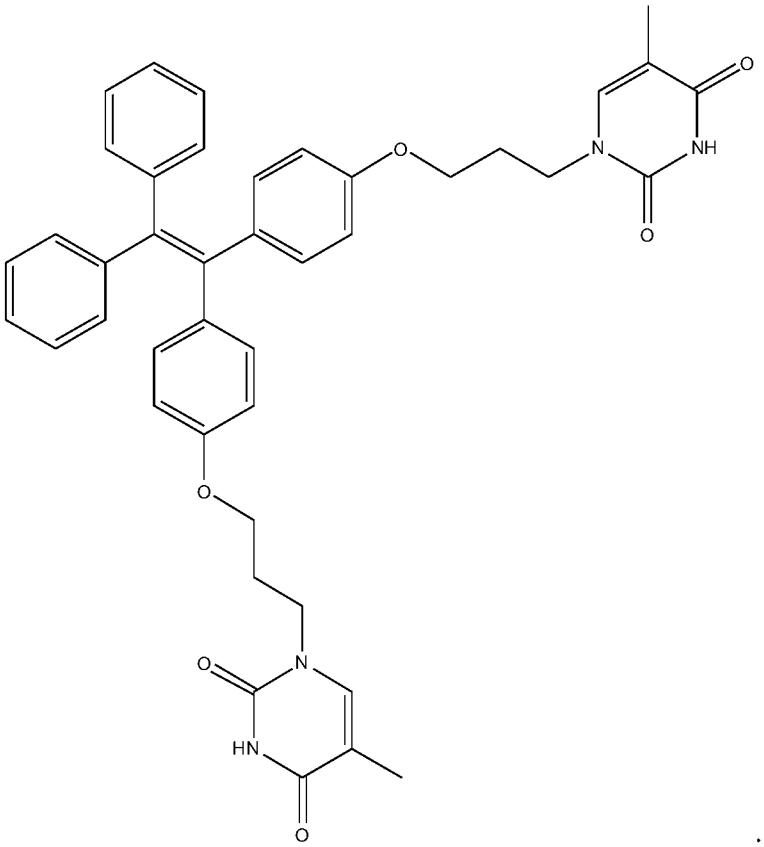
Modification	**Structure**
Poly(6-9)ethylene glycol (Peg)	
Octyldimethyl (ODM)	
Octyldimethyl + Peg 100,000	ODM + Poly(ethylene oxide) (average MW 100,000) grafted under radical conditions
Octyldimethyl + Peg 400,000	ODM + Poly(ethylene oxide) (average MW 400,000) grafted under radical conditions
Octyldimethyl + Peg 600,000	ODM + Poly(ethylene oxide) (average MW 600,000) grafted under radical conditions
Octyldimethyl + Peg 1,000,000	ODM + Poly(ethylene oxide) (average MW 1,000,000) grafted under radical conditions
Octyldimethyl + PVP 1,300,000	ODM + Polyvinylpyrrolidone (average MW 1,300,000) grafted under radical conditions
3-(dimethylaminopropyl)	
3-(aminopropyl)	
Perfluorooctyl	

Modification	Structure
Perfluorodecyl	
3-(trifluoromethyl)propyl	
3-cyanopropyl	
Propylmethacrylate	
3-mercaptopropyl	
3-mercaptopropyl + Peg 5000 Maleimide	
3-mercaptopropyl + acrylamide	
3-mercaptopropyl + trimethylammonium	
Zwitterionic sultone	

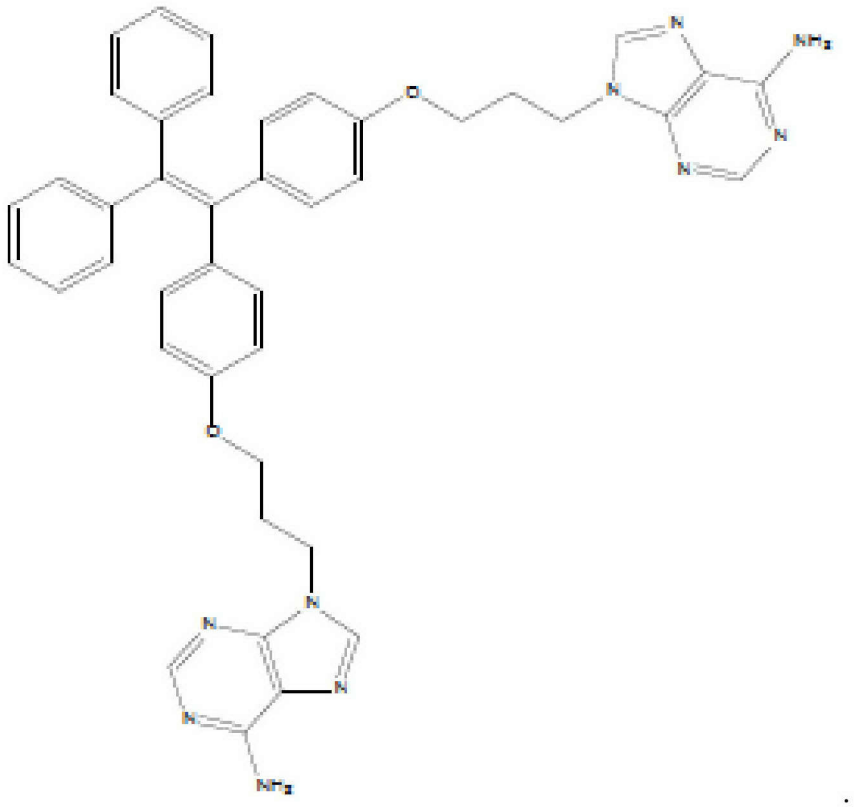
Modification	Structure
Zwitterionic phosphate	

III. Exemplary analyte detection techniques

[0154] Exemplary techniques enable detection of one or more analytes of interest in a sample using one or more sensor compounds. Exemplary techniques may use one or more sensor compounds that are known to interact with an analyte, if present in the sample, to cause production of an aggregate. Exemplary techniques enable detection of mercury (II) or silver (I) ions in a sample using one or more sensor compounds (e.g., TPET2 for mercury detection, or TPEA2 for silver detection). In certain cases, TPET2 molecules and mercury (II) ions interact to form an aggregate that substantially blocks fluid flow in the channel and consequently causes an electrical current and conductivity to decrease. TPET2 has the following molecular formula: $C_{42}H_{40}N_4O_6$. TPET2 has the following structure:



[0155] In certain cases, TPEA2 molecules and silver (I) ions interact to form an aggregate that substantially blocks fluid flow in the channel and consequently causes an electrical current and conductivity to decrease. TPEA2 has the following structure:



[0156] In certain embodiments, the electrodes used in the detection system may be metallic, for example, aluminum, manganese and platinum.

[0157] Exemplary techniques may introduce both the sample and the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection) into a channel in the detection system that is especially configured and dimensioned to allow analyte (e.g., mercury or silver) detection. In certain embodiments, the channel may be configured so that its depth and/or its width are substantially equal to or lower than a diameter of the aggregate particle. Upon introduction of both the sample and the sensor compound into the channel, formation of the aggregate may indicate presence of the analyte (e.g., mercury or silver) in the sample, while absence of the aggregate may indicate absence of the analyte (e.g., mercury or silver) in the sample.

[0158] When flow of the fluid and/or flow of the charged particles in the fluid is uninhibited (for example, due to absence of an aggregate), the conductive particles or ions in

the fluid (e.g., analyte particles or ions) may travel along at least a portion of the length of a channel in a detection system along the y-axis from an input port toward an output port. The movement of the conductive particles or ions may result in a first or "reference" electrical property value or range of values (e.g., of an electrical current, conductivity, resistivity) being detected (for example, by an analyte detection circuit) along at least a portion of the length of the channel. In some embodiments, electrical property values may be continually or periodically monitored during a time period until the values reach equilibrium (for example, by an equilibration circuit). One of the detected values may be selected as the reference electrical property value to avoid the influence of transient changes in the electrical property.

[0159] The term "reference" electrical property value may refer to a value or range of values of an electrical property of a channel prior to introduction of both a sample and a sensor compound in the channel. That is, the reference value is a value characterizing the channel prior to any interaction between analyte (e.g., mercury or silver) in the sample and the sensor compound. In some cases, the reference value may be detected at a time period after introduction of the sensor compound into the channel but before introduction of the sample into the channel. In some cases, the reference value may be detected at a time period after introduction of the sample into the channel but before introduction of the sensor compound into the channel. In some cases, the reference value may be detected at a time period before introduction of either the sample or the sensor compound into the channel. In some cases, the reference value may be predetermined and stored on a non-transitory storage medium from which it may be accessed.

[0160] However, when flow of the fluid and/or flow of the charged particles in the fluid is partially or completely blocked (for example, by formation of an aggregate), the conductive particles or ions in the fluid (e.g., analyte particles or ions) may be unable to freely travel along at least a portion of the length of the channel along the y-axis from the input port toward the output port. The hindered or stopped movement of the conductive particles or ions may result in a second electrical property value or range of values (e.g., of an electrical current, conductivity, resistivity) being detected along at least a portion of the length of the channel. In some embodiments, a waiting or adjustment time period may be allowed to pass after introduction of both the sample and the sensor compound into the channel prior to detecting the second electrical property value. The waiting or adjustment

time period allows an aggregate to form in the channel and for the aggregate formation to alter the electrical properties of the channel.

[0161] In some embodiments, one or more electrical property values may be continually or periodically monitored during a time period after the introduction of both the sample and the sensor compound until the values reach equilibrium. One of the detected values may be selected as the second electrical property value to avoid the influence of transient changes in the electrical property.

[0162] The second electrical property value may be compared to the reference electrical property value. If it is determined that the difference between the second value and the reference value corresponds to a predetermined range of decrease in current or conductivity (or increase in resistivity), it may be determined that an aggregate is present in the channel and that, therefore, the analyte of interest (e.g., mercury or silver) is present in the sample.

[0163] In some cases, formation of an electrically conductive aggregate may enhance the electrical pathway along at least a portion of the length of the channel. In this case, a third electrical property value or range of values (e.g., of an electrical current, conductivity, resistivity) may be detected along at least a portion of the length of the channel. In some embodiments, a waiting or adjustment time period may be allowed to pass after introduction of both the sample and the sensor compound into the channel prior to detecting the third electrical property value. The waiting or adjustment time period allows an aggregate to form in the channel and for the aggregate formation to alter the electrical properties of the channel.

[0164] In some embodiments, one or more electrical property values may be continually or periodically monitored during a time period after the introduction of both the sample and the sensor compound until the values reach equilibrium. One of the values may be selected as the third electrical property value to avoid the influence of transient changes in the electrical property.

[0165] The third electrical property value may be compared to the reference electrical property value. If it is determined that the difference between the third value and the reference value corresponds to a predetermined range of increase in current or

conductivity (or decrease in resistivity), it may be determined that an aggregate is present in the channel and that, therefore, the analyte of interest is present in the sample.

[0166] In certain embodiments, prior to use of a detection system, the channel may be free of the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection). That is, a manufacturer of the detection system may not pre-treat or modify the channel to include the sensor compound. In this case, during use, a user may need to introduce both the sensor compound and the sample into the channel.

[0167] In one example, the user may introduce the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection) and the sample into the channel concurrently, for example, in a mixture of the sensor compound and the sample. In this case, a reference electrical property value may be detected in the channel prior to introduction of the mixture, and an electrical property value may be detected after introduction of the mixture. Comparison of the electrical property value to the reference electrical property value may be used to determine if an analyte (e.g., mercury or silver) is present in the sample.

[0168] In another example, the user may introduce the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection) and the sample into the channel concurrently, for example, in a mixture of the sensor compound and the sample. A stored reference electrical property value characterizing the channel prior to introduction of both the sample and the sensor compound may be retrieved or accessed from a non-transitory storage medium. An electrical property value may be detected after introduction of the mixture of the sample and the sensor compound into the channel. Comparison of the electrical property value to the stored reference electrical property value may be used to determine if an analyte (e.g., mercury or silver) is present in the sample.

[0169] In another example, the user may first introduce the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection) into the channel, and detect a reference electrical property value with only the sensor compound in the channel. The user may subsequently introduce the sample into the channel, and detect an electrical property value after waiting for a time period after introduction of the sample into the channel. Comparison of the electrical property value to the reference electrical property value may be used to determine if an analyte (e.g., mercury or silver) is present in the sample.

[0170] In another example, the user may first introduce the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection) into the channel, and may subsequently introduce the sample into the channel. The user may then detect an electrical property value after waiting for a time period after introduction of the sample into the channel. A stored reference electrical property value characterizing the channel prior to introduction of both the sample and the sensor compound may be retrieved or accessed from a non-transitory storage medium. Comparison of the stored electrical property value to the reference electrical property value may be used to determine if an analyte (e.g., mercury or silver) is present in the sample.

[0171] In another example, the user may first introduce the sample into the channel, and detect a reference electrical property value with only the sample in the channel. The user may subsequently introduce the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection) into the channel, and detect an electrical property value after waiting for a time period after introduction of the sensor compound into the channel. Comparison of the electrical property value to the reference electrical property value may be used to determine if an analyte (e.g., mercury or silver) is present in the sample.

[0172] In another example, the user may first introduce the sample into the channel, and may subsequently introduce the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection) into the channel. The user may then detect an electrical property value after waiting for a time period after introduction of the sensor compound into the channel. A stored reference electrical property value characterizing the channel prior to introduction of both the sample and the sensor compound may be retrieved or accessed from a non-transitory storage medium. Comparison of the stored electrical property value to the reference electrical property value may be used to determine if an analyte (e.g., mercury or silver) is present in the sample.

[0173] In certain other embodiments, prior to use of the detection system, the channel may be pre-treated or modified so that at least a portion of an inner surface of the channel includes or is coated with the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection). That is, a manufacturer of the detection system may pre-treat or modify the channel to include the sensor compound. In this case, a user may only need to introduce the sample into the channel.

[0174] In one example, the manufacturer may detect a reference electrical property value of the channel with the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection) and may store the reference electrical property value on a non-transitory storage medium. During use, the user may introduce the sample into the channel and detect an electrical property value after waiting for a time period after introduction of the sample into the channel. The stored reference electrical property value may be accessed or retrieved from the storage medium. Comparison of the electrical property value to the reference electrical property value may be used to determine if an analyte (e.g., mercury or silver) is present in the sample.

[0175] In another example, the user may detect a reference electrical property value of the channel with the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection) prior to introducing the sample into the channel. The user may subsequently introduce the sample into the channel and detect an electrical property value after waiting for a time period after introduction of the sample into the channel. Comparison of the electrical property value to the reference electrical property value may be used to determine if an analyte (e.g., mercury or silver) is present in the sample.

[0176] Figures 7A and 7B are flowcharts illustrating an exemplary method 700 for detecting the presence or absence of an analyte (e.g., mercury or silver) in a sample. In step 702, a sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection) in an electrolyte buffer may be introduced into the channel using any suitable technique, for example, capillary filing or electro-kinetic filling. Alternatively, in step 702, at least a portion of an inner surface of the channel may be treated to include or be coated with the sensor compound (e.g., TPET2 for mercury detection, or TPEA2 for silver detection). In step 704, a potential difference may be applied across at least a portion of the length of the channel using a voltage source. In step 706, while the potential difference is being applied, one or more electrical properties values (e.g., the electrical current and/or conductivity) along at least a portion of the length of the channel may be detected. In some cases, the electrical current and/or conductivity may be directly measured. In other cases, a measure indicating the electrical current and/or a measure indicating the electrical conductivity may be detected.

[0177] Introduction of the sensor compound into the channel may cause transient changes in the electrical properties of the channel. In order to obtain an accurate and reliable

measure of the electrical properties, in step 708, a first set of two or more values that were detected in step 706 may be continually or periodically monitored. It may be determined if the electrical property values have reached equilibrium, i.e., has stopped varying outside of a predetermined variance or tolerance range. If it is determined that the electrical property values have not reached equilibrium, then the method may return to step 706 to detect additional electrical property values. On the other hand, if it is determined that the electrical property values have reached equilibrium, then the method may proceed to step 710.

[0178] In step 710, a first or reference value may be selected from the first set of electrical property. The first electrical property value may be used to represent the one or more electrical properties (e.g., electrical current or conductivity) of the channel prior to any introduction of both of the sample and the sensor compound into the channel.

[0179] In an alternative embodiment, the first value or reference value may be accessed from a non-transitory storage or memory, and may not need to be detected in steps 704-710, thereby making steps 704-710 unnecessary in this embodiment.

[0180] In step 711, in some embodiments, the electrolyte buffer including the TPET2 molecules or the TPEA2 molecules may be removed from the input port of the channel at which it was introduced. This step ensures that subsequent introduction of the sample at the input port does not cause interaction between the TPET2 molecules or the TPEA2 molecules, and the sample at the input port. This step ensures that, rather, any such interaction takes place within the length of the channel and not at the input port.

[0181] In step 712, a sample in an electrolyte buffer may be introduced into the channel using any suitable technique, for example, capillary filing or electro-kinetic filling.

[0182] Although the method illustrated in Figures 7A and 7B indicates that the sensor compound is introduced into the channel prior to introduction of the sample, another embodiment of the method may involve introducing the sample into the channel prior to introduction of the sensor compound. That is, the sample may be introduced into the channel in step 702 and the sensor compound may be introduced into the channel in step 712. Yet another embodiment may involve pre-mixing the sample and the sensor compound, and introducing the pre-mixture at one time into the channel. In the pre-mixing case, a reference electrical property value may be detected prior to introduction of the pre-mixture into the channel, and a second electrical property value may be detected after introduction of the pre-

mixture into the channel. The second value may be compared to the reference value to determine if an analyte (e.g., mercury or silver) is present in the sample.

[0183] In step 714, a potential difference may be applied across at least a portion of the length of the channel using a voltage source. In step 716, while the potential difference is being applied, one or more electrical properties (e.g., electrical current and/or conductivity) along at least a portion of the length of the channel may be detected. In some cases, the electrical current and/or conductivity may be directly measured. In other cases, a measure indicating the electrical current and/or a measure indicating the electrical conductivity may be detected.

[0184] Introduction of the sample into the channel may cause transient changes in the electrical current conducted along the channel. In order to obtain an accurate and reliable measure of the electrical properties, in step 718, a second set of two or more values that were detected in step 716 may be continually or periodically monitored. It may be determined if the electrical property values have reached equilibrium, e.g., has stopped temporally varying outside of a predetermined variance or tolerance range. If it is determined that the electrical property values have not reached equilibrium, then the method may return to step 716 to detect additional values. On the other hand, if it is determined that the electrical property values have reached equilibrium, then the method may proceed to step 720. In step 720, a second value may be selected from the second set of values of the electrical property. The second value may be used to represent the one or more electrical properties (e.g., electrical current or conductivity) along at least a portion of the length of the channel after both the sample and the sensor compound have been introduced into the channel.

[0185] In step 722, a difference between the magnitude of the first or reference value (determined in step 710) and the magnitude of the second value (determined in step 720) may be determined. In step 724, it may be determined if the difference determined in step 722 satisfies a predetermined threshold, for example, if the difference is above a predetermined value or if the difference is within a predetermined range.

[0186] If the sample includes a particular analyte (e.g., mercury or silver) that undergoes a particular type of interaction with the sensor compound, introduction of both the sample and the sensor compound into the channel may cause the particular type of interaction. Conversely, if the sample does not include the particular analyte (e.g., mercury or

silver), introduction of both the sample and the sensor compound into the channel may not cause the particular type of interaction. Thus, if the particular interaction causes a change in an electrical current or conductivity in the channel, then detection of the expected change in step 724 may indicate presence of the analyte (e.g., mercury or silver) in the sample.

[0187] As such, if it is determined in step 724 that the difference between the first and second values is greater than the predetermined threshold, then it may be determined in step 730 that the sample contains the analyte that is being tested for (e.g., mercury or silver). Subsequently, in step 732, an indication that the sample contains the analyte (e.g., mercury or silver) may be stored on a non-transitory storage medium. Alternatively or additionally, in step 732, an indication that the sample contains the analyte (e.g., mercury or silver) may be displayed on a display device.

[0188] On the other hand, if it is determined in step 724 that the difference between the first and second values is lower than the predetermined threshold, then it may be determined in step 726 that the sample does not contain the analyte that is being tested for. (e.g., mercury or silver). Subsequently, in step 728, an indication that the sample does not contain the analyte (e.g., mercury or silver) may be stored on a non-transitory storage medium. Alternatively or additionally, in step 728, an indication that the sample does not contain the analyte (e.g., mercury or silver) may be displayed on a display device.

[0189] Exemplary thresholds may include, but are not limited to, 5-100 nA in certain non-limiting cases.

[0190] With regards to mercury detection, exemplary thresholds may include, but are not limited to, 5-100 nA in certain non-limiting cases. In one example, a 100-nm channel may be capillary filled with an electrolyte buffer (e.g., sodium tetraborate dissolved in water and acetonitrile with a ratio of 2:1 50 mM sodium tetraborate:acetonitrile) for approximately five minutes by addition of approximately 10 μL of electrolyte buffer to one of the channel ports. Upon complete channel filling, approximately 10 μL of electrolyte buffer may be added to the other channel port and electrodes connected to a Kiethley 2410 ammeter are then inserted into the ports of the channel and a differential of +500 V or -500 V is applied until a stable current is obtained (approximately 29 to 31 nA for +500 V and approximately -29 to -31 nA for -500 V). Approximately 2μL of solution containing 100 μM mercury (II) nitrate monohydrate (which is the analyte) in electrolyte buffer (2:1 50 mM sodium

borate:acetonitrile) and a differential of +500 V or -500 V volts may be applied until a stable current is obtained (approximately 28 to 29 nA for +500 V and approximately -29 to -31 nA for -500 V). The sample mercury nitrate in buffer may be removed from the ports of the channel to be replaced by approximately 5 μL of a solution containing 20 μM of TPET2 in electrolyte buffer (2:1 50 mM sodium borate:acetonitrile) is added to each channel port. The electric field may be intermittently switched between +500 V and -500 V to induce mixing at 30-second cycles. Stable currents of different magnitudes may be detected regardless of the direction of the electric field (approximately 29 to 33 nA for +500 V and approximately -37 to -40 nA for -500 V).

[0191] With regards to silver detection, exemplary thresholds may include, but are not limited to, 5-100 nA in certain non-limiting cases. In one example, a 100-nm channel may be capillary filled with an electrolyte buffer (e.g., sodium tetraborate dissolved in water and tetrahydrofuran with a ratio of 5:1 45 mM sodium tetraborate: tetrahydrofuran) for approximately five or ten minutes by addition of approximately 10 μL of electrolyte buffer to one of the channel ports. Upon complete channel filling, approximately 10 μL of electrolyte buffer is added to the other channel port and electrodes connected to a Kiethley 2410 ammeter are then inserted into the ports of the channel and a differential of +1000 V or -1000 V is applied until a stable current is obtained (approximately 45 nA for +1000 V and approximately -45 nA for -1000 V). Approximately 40 μM TPEA2 in 5:1 50 mM borate:tetrahydrofuran is introduced into the channel and a potential differential of +1000 V or -1000 V volts is applied until a stable current is obtained (approximately 40 to 43 nA for +1000 V and approximately -40 to -43 nA for -1000 V). The TPEA2 buffer may be removed from just one or both channel ports and replaced with approximately 5 μL of a sample solution. The sample solution may or may not contain silver ions. In one example, if the sample solution is one that contains silver ions, the sample solution may contain approximately 200 μM silver (I) nitrate in electrolyte buffer (approximately 5:1 ratio of 50 mM sodium borate:tetrahydrofuran). After the sample solution is introduced into the channel, a potential difference of a +1000 V may be applied across the electrodes and the field is intermittently switched to -1000 V to induce mixing. Approximately 30 second cycles may be used at +1000 V and -1000 V to induce sample mixing, and the electrical current along at least a portion of the length of the channels may be detected at both applied fields. With an

applied field of approximately +1000 V, electrical current of approximately 43 to 46 nA is detected in certain cases, and with an applied field of -1000 V, electrical current of approximately -60 to -63 nA is detected in certain cases.

[0192] In certain embodiments, the channel may be prepared for reuse for subsequent testing of samples. In step 736, a de-aggregation agent may be introduced into the channel using any suitable technique, for example, capillary filing or electro-kinetic filling. The de-aggregation agent may be selected so that interaction between the de-aggregation agent and the aggregate formed in the channel causes the aggregate to dissolve or disintegrate. Subsequently, the channel may be filled with an electrolyte buffer to flush out the channel and allow a sample and a sensor compound to be introduced into the channel. In one example, a channel including an aggregate may be prepared for reuse by washing the channel with dimethylsulfoxide introduced into the channel with a potential difference of 500 V applied between the input and output nodes, followed by washing with 10 mM sodium hydroxide introduced into the channel with a potential difference of 500 V applied between the input and output nodes, followed by washing with 1 M hydrogen chloride introduced into the channel with a potential difference of 100 V applied between the input and output nodes. In another example, a channel including an aggregate may be prepared for reuse by washing the channel with dimethylsulfoxide introduced into the channel for ten minutes with a potential difference of 500 V applied between the input and output nodes, followed by washing with 1 M hydrogen chloride introduced into the channel for 10 minutes with a potential difference of 100 V applied between the input and output nodes, followed by washing with 100 mM sodium tetraborate introduced into the channel for 10 minutes with a potential difference of 500 V applied between the input and output nodes, followed by 18 MilliQ MegaOhm water introduced into the channel for 10 minutes with a potential difference of 500 V applied between the input and output nodes.

[0193] In certain embodiments, in step 734, prior to disintegration of the aggregate, an absolute or relative concentration of an analyte (e.g., mercury or silver) may be determined based on an electrical property value of the channel. The concentration of an analyte may be determined in such a manner because the channels of exemplary detection systems have a high inner surface area to volume ratio. At low concentrations of the analyte, electrical conductivity in the channel is dominated by surface charges. As such,

measurements of electrical properties of the channel can enable distinction between different ions. As a result, unique and sensitive measurements of the bulk flow in the channel can be used to determine information on the surface charges at the inner surface of the channel. Exemplary embodiments may thus compute predetermined ranges of electrical property values of the channel that are characteristic of a particular analyte ion (e.g., mercury or silver ions) given the dimensions of the channel and at different concentrations of the analyte ion. These predetermined values may then be used to determine an unknown concentration of an analyte in a sample. Detailed information on surface charges in the channel for different ions is presented in the following papers, the entire contents of which are expressly incorporated herein by reference: "Surface-dependent chemical equilibrium constants and capacitances for bare and 3- cyanopropyldimethylchlorosilane coated silica nanochannels" M. B. Andersen, J. Frey, S. Pennathur and H. Bruus, J. Colloid Interface Sci. 353, 301-310 (2011), and "Hydronium-domination ion transport in carbon-dioxide-saturated electrolytes at low salt concentrations in nanochannels" K.L. Jensen, J.T. Kristensen, A.M. Crumrine, M.B.Andersen, H. Bruus and S. Pennathur. Phys. Review E. 83, 5, 056307.

[0194] Figure 5 is a schematic drawing of the inside of a channel including an inner surface of the channel 502, an immobile layer of fluid 504 lying immediately adjacent to the inner surface of the channel, a diffusive layer of fluid 506 lying immediately adjacent to the immobile layer, and a bulk fluid flow layer 508 lying immediately adjacent to the diffusive layer. Exemplary ions are represented in each of the fluid layers. Upon application of a potential difference across the length of the channel, an electrical property value may be detected along at least a portion of the channel (for example, by the analyte detection circuit 122). The comparison circuit 124 may be used to compare the measured electrical property value to a predetermined range of electrical property values that correspond to a particular concentration or range of concentration values of the analyte (e.g., mercury or silver). The concentration determined may be an absolute concentration of the analyte (e.g., mercury or silver) or a relative concentration of the analyte (e.g., mercury or silver) with respect to the concentrations of one or more other substances in the channel.

[0195] Figures 6A and 6B are graphs showing conductivity values measured in a channel for different test cases. In each test case, a different relative concentration of an analyte relative to concentrations of two additional substances (in this case, ammonium and

hydrogen peroxide) is used, and the corresponding conductivity value is determined in the channel. In one embodiment, Standard Clean 1 or SC1 is used a solution in the test cases. Details of SC1 can be found online. The ratios of concentrations among the three substances in the test cases represented in Figures 6A and 6B are presented in Table 1 above.

[0196] The lower the concentration of an analyte, the easier it is to measure differences in relative concentrations between the analyte and other substances. For example, at concentration ratios of 1000:1:1, detection sensitivity on the order of 1-10 ppm may be achieved in the exemplary detection system. At concentration ratios of 350:1:1, detection sensitivity on the order of 100 ppm may be achieved. At concentration ratios of 5:1:1, detection sensitivity on the order of 10,000 ppm may be achieved.

[0197] Another exemplary technique for detecting the analyte (e.g., mercury or silver ions) may involve detection of the presence of a diode-like behavior in the channel that is caused by the formation of the analyte aggregate in the channel. In the absence of an aggregate, application of a potential difference having a substantially similar magnitude (e.g., +500 V) may result in a substantially same magnitude of an electrical property (e.g., current) detected along the length of the channel regardless of the direction of application of the potential difference or electric field. If the potential difference is applied across the length of the channel in a first direction along the length of the channel (e.g., such that the positive electrode is at an input port 110 at or near a first end of the channel and such that the negative electrode is at an output port 112 at or near a second end of the channel), the resulting current may be substantially equal in magnitude to the resultant current if the potential difference is applied in the opposite direction (e.g., such that the positive electrode is at the output port 112 and such that the negative electrode is at the input port 110).

[0198] Formation of an aggregate in the channel may cause a diode-like behavior in which reversal of the direction of the applied potential difference or electric field causes a change in the electrical property detected in the channel. The diode-like behavior causes the detected electrical current to vary in magnitude with the direction of the electric field. When the electric field or potential difference is applied in the first direction, the magnitude of the electrical current may be different in magnitude than when the potential different or electric field is applied in the opposite direction. Thus, comparison between a first electrical property value (detected when a potential difference is applied in a first direction along the channel

length) and a second electrical property value (detected when a potential difference is applied in a second opposite direction along the channel length) may enable detection of an aggregate, and thereby detection of the analyte (e.g., mercury or silver ions) in the sample. If the first and second electrical property values are substantially equal in magnitude, then it may be determined that the sample does not contain the analyte (e.g., mercury or silver ions). On the other hand, if the first and second electrical property values are substantially unequal in magnitude, then it may be determined that the sample contains the analyte (e.g., mercury or silver ions). In other words, the sum of the values of the electrical property (positive in one direction, negative in the other direction) is substantially zero in the absence of an aggregate and substantially non-zero in the presence of an aggregate. Figures 8A and 8B are flowcharts illustrating a general exemplary method 750 for detecting the presence or absence of an analyte in a sample. In step 752, a sensor compound in an electrolyte buffer and a sample may be introduced into the channel using any suitable technique, for example, capillary filing or electro-kinetic filling. The sensor compound and the sample may be introduced concurrently or separately. In one embodiment, at least a portion of an inner surface of the channel may be treated to include or be coated with the sensor compound. In step 754, a potential difference may be applied across at least a portion of the length of the channel using a voltage source in a first direction along the channel length (y-axis). In step 756, while the potential difference is being applied, one or more electrical properties values (e.g., the electrical current and/or conductivity) along at least a portion of the length of the channel may be detected. In some cases, the electrical current and/or conductivity may be directly measured. In other cases, a measure indicating the electrical current and/or a measure indicating the electrical conductivity may be detected.

[0199] In order to obtain an accurate and reliable measure of the electrical properties, in step 758, a first set of two or more values that were detected in step 756 may be continually or periodically monitored. It may be determined if the electrical property values have reached equilibrium, e.g., has stopped varying outside of a predetermined variance or tolerance range. If it is determined that the electrical property values have not reached equilibrium, then the method may return to step 756 to detect additional electrical property values. On the other hand, if it is determined that the electrical property values have reached equilibrium, then the method may proceed to step 760.

[0200] In step 760, a first value may be selected from the first set of electrical property. The first electrical property value may be used to represent the one or more electrical properties (e.g., electrical current or conductivity) of the channel when an electric field is applied in a first direction along the channel length (y-axis).

[0201] In step 762, a potential difference may be applied across at least a portion of the length of the channel using a voltage source in a second opposite direction along the channel length (y-axis). The second direction may be substantially opposite to the first direction. In step 764, while the potential difference is being applied, one or more electrical properties (e.g., electrical current and/or conductivity) along at least a portion of the length of the channel may be detected. In some cases, the electrical current and/or conductivity may be directly measured. In other cases, a measure indicating the electrical current and/or a measure indicating the electrical conductivity may be detected.

[0202] In order to obtain an accurate and reliable measure of the electrical properties, in step 766, a second set of two or more values that were detected in step 764 may be continually or periodically monitored. It may be determined if the electrical property values have reached equilibrium, e.g., has stopped temporally varying outside of a predetermined variance or tolerance range. If it is determined that the electrical property values have not reached equilibrium, then the method may return to step 764 to detect additional values. On the other hand, if it is determined that the electrical property values have reached equilibrium, then the method may proceed to step 768. In step 768, a second value may be selected from the second set of values of the electrical property. The second value may be used to represent the one or more electrical properties (e.g., electrical current or conductivity) along at least a portion of the length of the channel after both the sample and the sensor compound have been introduced into the channel.

[0203] In step 770, a difference between the magnitude of the first value (determined in step 760) and the magnitude of the second value (determined in step 768) may be determined. In step 772, it may be determined if the difference determined in step 770 satisfies a predetermined threshold, for example, if the difference is above a predetermined value or if the difference is within a predetermined range.

[0204] If it is determined in step 772 that the difference between the first and second values satisfies the predetermined threshold (e.g., that the difference in magnitudes is

substantially non-zero), then it may be determined in step 778 that the sample contains the analyte that is being tested for (e.g., mercury or silver ions). Subsequently, in step 780, an indication that the sample contains the analyte may be stored on a non-transitory storage medium. Alternatively or additionally, in step 780, an indication that the sample contains the analyte may be displayed on a display device.

[0205] On the other hand, if it is determined in step 772 that the difference between the first and second values does not satisfy the predetermined threshold (e.g., that the difference in magnitudes is substantially zero), then it may be determined in step 774 that the sample does not contain the analyte that is being tested for (e.g., mercury or silver ions). Subsequently, in step 776, an indication that the sample does not contain the analyte may be stored on a non-transitory storage medium. Alternatively or additionally, in step 776, an indication that the sample does not contain the analyte (e.g., mercury or silver ions) may be displayed on a display device.

[0206] In certain cases, if the difference in magnitude between the first and second values is greater than the threshold, then it may be determined that the sample contains the analyte (e.g., mercury or silver ions). Otherwise, it may be determined that the sample does not contain the analyte (e.g., mercury (Hg) ions or silver (Ag) ions). In certain non-limiting examples, the threshold may be approximately 1 nA to approximately 3 nA.

[0207] In one example in which the presence of mercury (II) ions is detected by TPET2 (C42H40N4O6), interaction between the mercury ions and TPET2 result in the formation of an aggregate in the channel. In the absence of the mercury aggregate, the first and second electrical property values may be substantially equal. For example, when the channel is filled with a 2:1 50 mM borate:acetonitrile (lacking an aggregate), a first current value of 32 nA to 33 nA is detected when a potential difference of +500 V is applied in a first direction, and a second current value of -31 nA to -32 nA is detected when a potential difference of -500V is applied in a second opposite direction. Similarly, when the channel is filled with a 100 μM mercury (ii) nitrate solution in 2:1 50 mM borate:acetonitrile (lacking a sensor compound and lacking an aggregate), a first current value of 29 nA to 31 nA is detected when a potential difference of +500 V is applied in a first direction, and a second current value of 28 nA to 30 nA is detected when a potential difference of -500 V is applied in a second opposite direction. That is, the difference between the magnitudes of the two

electrical property values is substantially zero (e.g., 0 to 3 nA). In other words, the two electrical property values are substantially equal, indicating the absence of a mercury aggregate in the channel. In contrast, in the presence of a mercury aggregate in this example, the first and second electrical property values may be unequal, that is, substantially different. For example, when a mercury aggregate is present in the channel (after introduction of both the mercury-containing sample and TPET2 into the channel), a first current value of 29 nA to 33 nA is detected when a potential difference of +500 V is applied in a first direction, and a second current value of -37 nA to -40 nA is detected when a potential difference of -500V is applied in a second opposite direction. That is, the difference between the magnitudes of the two electrical property values is non-zero (e.g., 7 to 8 nA). In other words, the two electrical property values are substantially unequal, indicating the presence of a mercury aggregate in the channel.

[0208] In one example in which the presence of silver (I) ions is detected by TPEA2, interaction between the silver ions and TPEA2 result in the formation of an aggregate in the channel. In the absence of the silver aggregate, the first and second electrical property values may be substantially equal. For example, when the channel is filled with a 5:1 45 mM sodium tetraborate:tetrahydrofuran (lacking an aggregate), a first current value of 45 nA may be detected when a potential difference of +1000 V is applied in a first direction, and a second current value of -45 nA may be detected when a potential difference of -1000 V is applied in a second opposite direction. Similarly, when the channel is filled with a 40 μM TPEA2 in 5:1 50 mM borate:tetrahydrofuran (lacking a sensor compound and lacking an aggregate), a first current value of 40 nA to 43 nA may be detected when a potential difference of +1000 V is applied in a first direction, and a second current of -40 nA to -43 nA may be detected when a potential difference of -1000V is applied in a second opposite direction. That is, the difference between the magnitudes of the two electrical property values is substantially zero (e.g., 0 to 3 nA). In other words, the two electrical property values are substantially equal, indicating the absence of a silver aggregate in the channel. In contrast, in the presence of a silver aggregate in this example, the first and second electrical property values may be unequal, that is, substantially different. For example, when a silver aggregate is present in the channel (after introduction of both the silver-containing sample and TPEA2 into the channel), a first current value of 43 nA to 46 nA may be detected when a potential

difference of +1000 V is applied in a first direction, and a second current value of -60 nA to -63 nA may be detected when a potential difference of -1000V is applied in a second opposite direction. That is, the difference between the magnitudes of the two electrical property values is non-zero. In other words, the two electrical property values are substantially unequal, indicating the presence of a silver aggregate in the channel.

[0209] In certain embodiments, the channel may be prepared for reuse for subsequent testing of samples. In step 784, a de-aggregation agent may be introduced into the channel using any suitable technique, for example, capillary filing or electro-kinetic filling. The de-aggregation agent may be selected so that interaction between the de-aggregation agent and the aggregate formed in the channel causes the aggregate to dissolve or disintegrate. The channel may be filled with an electrolyte buffer to flush out the channel and allow a sample and a sensor compound to be introduced into the channel. In one example, a channel including an aggregate may be prepared for reuse by washing the channel with dimethylsulfoxide introduced into the channel with a potential difference of t 500 V applied between the input and output nodes, followed by washing with 10mM sodium hydroxide introduced into the channel with a potential difference of 500 V applied between the input and output nodes, followed by washing with 1 M hydrogen chloride introduced into the channel with a potential difference of 100 V applied between the input and output nodes. In another example, a channel including an aggregate may be prepared for reuse by washing the channel with dimethylsulfoxide introduced into the channel for ten minutes with a potential difference of 500 V applied between the input and output nodes, followed by washing with 1 M hydrogen chloride introduced into the channel for 10 minutes with a potential difference of 100 V applied between the input and output nodes, followed by washing with 100 mM sodium tetraborate introduced into the channel for 10 minutes with a potential difference of 500 V applied between the input and output nodes, followed by 18 MilliQ MegaOhm water introduced into the channel for 10 minutes with a potential difference of 500 V applied between the input and output nodes.

[0210] In certain embodiments, in step 782, prior to disintegration of the aggregate, an absolute or relative concentration of an analyte (e.g., mercury or silver ions) may be determined based on an electrical property value of the channel. The concentration of an analyte (e.g., mercury or silver ions) may be determined in such a manner because the

channels of exemplary detection systems have a high inner surface area to volume ratio. At low concentrations of the analyte (e.g., mercury or silver ions), electrical conductivity in the channel is dominated by surface charges. As such, measurements of electrical properties of the channel can enable distinction between different ions. As a result, unique and sensitive measurements of the bulk flow in the channel can be used to determine information on the surface charges at the inner surface of the channel. Exemplary embodiments may thus compute predetermined ranges of electrical property values of the channel that are characteristic of a particular analyte ion (e.g., mercury or silver ions) given the dimensions of the channel and at different concentrations of the analyte ion. These predetermined values may then be used to determine an unknown concentration of an analyte (e.g., mercury or silver ions) in a sample.

[0211] Figure 9 is a flowchart illustrating a general exemplary method 800 for detecting the presence or absence of an analyte (e.g. mercury or silver) in a sample. In step 802, a sample may be introduced into a channel of a detection system, the channel having a length and a width, the length substantially greater than the width. In step 804, an electrical property value of an electrical property (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of the channel after the sample is introduced into the channel. In step 806, a reference electrical property value may be accessed. The reference electrical property value may be associated with the electrical property detected in step 804 along at least a portion of the length of the channel prior to introduction of the sample into the channel. In step 808, the electrical property value measured in step 804 may be compared to the reference electrical property value accessed in step 806. In step 810, based on the comparison in step 808, presence or absence of an analyte (e.g., mercury or silver) in the sample may be determined.

[0212] Figure 10 is a flowchart illustrating a general exemplary method 900 for detecting the presence or absence of an analyte (e.g., mercury or silver) in a sample. In step 902, one or more electrical property values of one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of a channel, the channel having a length and a width, the length substantially greater than the width. In step 904, a reference channel electrical property value may be determined based on the electrical property values of the channel measured in step 902. In step 906, a sample may be

introduced into the channel. In step 908, one or more electrical property values of one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of the channel after introduction of the sample into the channel. In step 910, a sample channel electrical property value may be determined based on the one or more electrical property values measured in step 908. In step 912, the sample channel electrical property value determined in step 910 may be compared to the reference channel electrical property value determined in step 904. In step 914, based on the comparison in step 912, presence or absence of an analyte (e.g., mercury or silver) in the sample may be determined.

[0213] Figure 11 is a flowchart illustrating a general exemplary method 1000 for detecting the presence or absence of an analyte (e.g., mercury or silver) in a sample. In step 1002, a mixture of a sample and a sensor compound may be introduced into a channel, the channel having a length and a width, the length substantially greater than the width. In step 1004, an electrical property value of an electrical property (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of the channel after the sample and the sensor compound are introduced into the channel. In step 1006, a reference electrical property value may be accessed. The reference electrical property value may be associated with the electrical property detected in step 1004 along at least a portion of the length of the channel prior to introduction of the sample and the sensor compound into the channel. In step 1008, any differences between the electrical property value measured in step 1004 and the reference electrical property value accessed in step 1006 may be determined. In step 1010, based on the differences, if any, determined in step 1008, presence or absence of an analyte (e.g., mercury or silver) in the sample may be determined.

[0214] Figure 12 is a flowchart illustrating a general exemplary method 1100 for detecting the presence or absence of an analyte (e.g., mercury or silver) in a sample. In step 1102, a sensor compound may be introduced into a channel, the channel having a length and a width, the length substantially greater than the width. In step 1104, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of a channel. In step 1106, a reference channel electrical property value may be determined based on the electrical properties of the channel measured in step 1104. In step 1108, a sample may be introduced into the channel. In step 1110, one or more electrical

properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of a channel. In step 1112, an electrical property value of the channel may be determined based on the one or more electrical properties measured in step 1110. In step 1114, any differences between the electrical property value determined in step 1112 and the reference channel electrical property value determined in step 1106 may be determined. In step 1116, based on the differences, if any, determined in step 1114, presence or absence of an analyte (e.g., mercury or silver) in the sample may be determined.

[0215] Figure 13 is a flowchart illustrating a general exemplary method 1200 for detecting the presence or absence of an analyte (e.g., mercury or silver) in a sample. In step 1202, a sensor compound may be introduced into a channel, the channel having a length and a width, the length substantially greater than the width. In step 1204, a sample may be introduced into the channel. In step 1206, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of a channel. In step 1208, an electrical property value of the channel may be determined based on the one or more electrical properties measured in step 1206. In step 1210, a reference channel electrical property value may be accessed. The reference channel electrical property value may be measured prior to introduction of both the sensor compound and the sample into the channel. In step 1212, any differences between the electrical property value determined in step 1208 and the reference channel electrical property value accessed in step 1210 may be determined. In step 1214, based on the differences, if any, determined in step 1212, presence or absence of an analyte (e.g., mercury or silver) in the sample may be determined.

[0216] Figure 14 is a flowchart illustrating a general exemplary method 1300 for detecting the presence or absence of an analyte (e.g., mercury or silver ions) in a sample. In step 1302, a sample may be introduced into a channel of a detection system, the channel having a length and a width, the length substantially greater than the width. In step 1304, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of the channel after the sample is introduced into the channel. In step 1306, a reference channel electrical property value may be determined based on the one or more electrical properties measured in step 1304. In step 1308, a sensor compound may be introduced into the channel. In step 1310, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of

the channel after the sensor compound is introduced into the channel. In step 1312, an electrical property value may be determined based on the one or more electrical properties measured in step 1310 after the sensor compound and the sample are introduced into the channel. In step 1314, any differences between the electrical property value determined in step 1312 and the reference channel electrical property value determined in step 1306 may be determined. In step 1316, based on the differences, if any, determined in step 1314, presence or absence of an analyte (e.g., mercury or silver) in the sample may be determined.

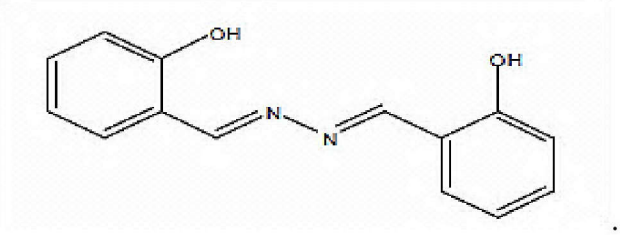
[0217] Figure 15 is a flowchart illustrating a general exemplary method 1400 for detecting the presence or absence of an analyte (e.g., mercury or silver) in a sample. In step 1402, a sample may be introduced into a channel of a detection system, the channel having a length and a width, the length substantially greater than the width. In step 1404, a sensor compound may be introduced into the channel. In step 1406, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of the channel after the sample and the sensor compound are introduced into the channel. In step 1408, an electrical property value may be determined based on the one or more electrical properties measured in step 1406 after the sensor compound and the sample are introduced into the channel. In step 1410, a reference channel electrical property value may be accessed. The reference channel electrical property value may be measured prior to introduction of both the sensor compound and the sample into the channel. In step 1412, any differences between the electrical property value determined in step 1408 and the reference channel electrical property value accessed in step 1410 may be determined. In step 1414, based on the differences, if any, determined in step 1412, presence or absence of an analyte (e.g., mercury or silver) in the sample may be determined.

[0218] Figure 16 is a flowchart illustrating a general exemplary method 1500 for detecting the presence or absence of an analyte (e.g., mercury or silver) in a sample. In step 1502, at least a portion of an inner surface of a channel may be coated with a sensor compound. The channel may have a length and a width, the length substantially greater than the width. In some cases, the inner portion of the channel may be pre-treated or covalently modified to enable specific covalent attachment of the sensor compound to the inner surface and to prevent non-specific attachment of other molecules to the inner surface. In step 1504, one or more electrical properties (e.g., current, conductivity, resistance) may be measured

along at least a portion of the length of a channel. In step 1506, a reference channel electrical property value may be determined based on the one or more electrical properties measured in step 1504. In step 1508, the reference channel electrical property value may be stored on a non-transitory storage medium for use in determining whether the analyte (e.g., mercury or silver) is present or absent in the sample.

IV. Exemplary technique for detection of a solvent

[0219] The exemplary detection systems and techniques may be configured to detect the presence or absence of a particular solvent (e.g., water) in a sample. In this case, the analyte being tested in the sample is a solvent (e.g., water). An exemplary sensor compound that may be used to test for the presence or absence of the solvent is a dye that dissolves in ethanol but that forms an aggregate in water. That is, the dye and water interact to form an aggregate that substantially blocks fluid flow in the channel and consequently causes an electrical current and conductivity to decrease. An exemplary dye is salicylaldehyde azine (SA), which has the following structure:



[0220] Figures 17A and 17B are flowcharts illustrating an exemplary method 1600 for detecting a solvent in a sample. In step 1602, an electrolyte buffer may be introduced into a channel using any suitable technique, for example, capillary filing or electro-kinetic filling. The electrolyte buffer may be sodium hydroxide dissolved in ethanol. Any suitable concentration of sodium hydroxide in ethanol may be introduced into the channel including, but not limited to, 1-10 mM. In step 1606, a potential difference may be applied across at least a portion of the length of the channel using a voltage source.

[0221] In step 1608, a dye in an electrolyte buffer (e.g., SA dissolved in sodium hydroxide and ethanol) may be introduced into the channel using any suitable technique, for example, capillary filing or electro-kinetic filling. Any suitable concentration of sodium hydroxide in ethanol may be introduced into the channel including, but not limited to, 1-10

mM. Any suitable concentration of the dye may be introduced into the channel including, but not limited to, 1-50 μM. In step 1610, a potential difference may be applied across at least a portion of the length of the channel using a voltage source. In step 1612, while the potential difference is being applied, one or more electrical property values (e.g., current, conductivity, resistivity) along at least a portion of the length of the channel may be detected.

[0222] In order to obtain an accurate and reliable measure of the electrical current, in step 1614, an equilibration circuit may be used to analyze a first set of two or more values that were detected in step 1612. The equilibration circuit may determine if the values have reached equilibrium, i.e., have stopped varying outside of a predetermined variance or tolerance range. If it is determined that the values have not reached equilibrium, then the method may return to step 1612 to detect additional values. On the other hand, if it is determined that the values have reached equilibrium, then the method may proceed to step 1616. In step 1616, the equilibration circuit may select a first or reference value from the first set of values. The first or reference value may be used to represent one or more electrical properties of the channel prior to interaction between the sample and the dye.

[0223] In step 1618, in some embodiments, the electrolyte buffer including the dye molecules may be removed from the input port of the channel at which it was introduced. This step ensures that subsequent introduction of the sample at the input port does not cause interaction between the dye molecules and the sample at the input port.In step 1620, the sample may be introduced into the channel using any suitable technique, for example, capillary filing or electro-kinetic filling. In step 1622, a potential difference may be applied across at least a portion of the length of the channel using a voltage source. In step 1624, while the potential difference is being applied, one or more electrical property values (e.g., current, conductivity, resistivity) along at least a portion of the length of the channel may be detected.

[0224] In order to obtain an accurate and reliable measure of the electrical current, in step 1626, an equilibration circuit may be used to analyze a second set of one or more values that were detected in step 1624. The equilibration circuit may determine if the values have reached equilibrium, i.e., have stopped varying outside of a predetermined variance or tolerance range. If it is determined that the values have not reached equilibrium, then the method may return to step 1624 to detect additional values. On the other hand, if it is

determined that the values have reached equilibrium, the method may proceed to step 1628. In step 1628, the equilibration circuit may select a second value from the second set of values. The second value may be used to represent one or more electrical properties of the channel after any interaction between the sample and the dye.

[0225] In step 1630, a comparison circuit may be used to determine a difference between the first or reference value (determined in step 1616) and the second value (determined in step 1628). In step 1632, the comparison circuit may determine if the difference determined in step 1630 satisfies a predetermined threshold, for example, if the difference is above a predetermined value or if the difference is within a predetermined range.

[0226] If it is determined in step 1632 that the difference between the first and second values satisfies the predetermined threshold, then the analyte detection circuit may determine in step 1638 that the sample contains the solvent. Subsequently, in step 1640, the analyte detection circuit may store, on a non-transitory computer-readable medium, an indication that the sample contains the solvent. Alternatively or additionally, in step 1640, the analyte detection circuit may display, on a display device, an indication that the sample contains the solvent.

[0227] On the other hand, if it is determined in step 1632 that the difference between the first and second values does not satisfy the predetermined threshold, then the analyte detection circuit may determine in step 1634 that the sample does not contain the solvent. Subsequently, in step 1636, the analyte detection circuit may store, on a non-transitory computer-readable medium, an indication that the sample does not contain the solvent. Alternatively or additionally, in step 1636, the analyte detection circuit may display, on a display device, an indication that the sample does not contain the solvent.

[0228] In certain embodiments, the channel may be reused for subsequent testing of samples. In step 1644, a de-aggregation agent may be introduced into the channel using any suitable technique, for example, capillary filing or electro-kinetic filling. The de-aggregation agent may be selected so that interaction between the de-aggregation agent and the aggregate formed in the channel causes the aggregate to dissolve or disintegrate. The channel may be filled with an electrolyte buffer to flush out the channel and allow a sample and sensor compound to be introduced into the channel.

[0229] In certain embodiments, in step 1642, prior to disintegration of the aggregate, an absolute or relative concentration of the solvent may be determined based on an electrical property value of the channel, and the concentration may be stored on a non-transitory storage device and/or displayed on a visual display device. The concentration of an analyte may be determined in such a manner because the channel of the exemplary detection system has a high surface area to volume ratio. At low concentrations of the analyte, electrical conductivity in the channel is dominated by surface charges. As such, measurements of electrical properties of the channel can enable distinction between different ions. As a result, unique and sensitive measurements of the bulk flow in the channel can be used to determine the information on the surface charges at the inner surface of the channel. Exemplary embodiments thus compute predetermined ranges of electrical property values of the channel that are characteristic of a particular analyte ion given the dimensions of the channel and at different concentrations of the analyte ion. These predetermined values may then be used to determine the concentration of an analyte in a sample.

[0230] Detailed information on surface charges in the channel for different ions is presented in the following papers, the entire contents of which are expressly incorporated herein by reference: "Surface-dependent chemical equilibrium constants and capacitances for bare and 3- cyanopropyldimethylchlorosilane coated silica nanochannels" M. B. Andersen, J. Frey, S. Pennathur and H. Bruus, J. Colloid Interface Sci. 353, 301-310 (2011), and "Hydronium-domination ion transport in carbon-dioxide-saturated electrolytes at low salt concentrations in nanochannels" K.L. Jensen, J.T. Kristensen, A.M. Crumrine, M.B.Andersen, H. Bruus and S. Pennathur. Phys. Review E. 83, 5, 056307.

V. Exemplary nucleic acid detection techniques

[0231] Exemplary techniques enable detection of particular nucleic acids and/or nucleotides (e.g., DNA, RNA) in a sample using one or more sensor compounds (i.e., one or more nucleic acid probes). An exemplary nucleic acid that may be detected is glyceraldehyde-3-phosphate dehydrogenase (GAPD) messenger RNA (mRNA) included in a total RNA extract. One or more exemplary sensor compounds that may be used to test for the presence or absence of a nucleic acid include one or more nucleic acid probes that bind, directly or indirectly, with the analyte nucleic acid to form an electrically conductive

aggregate. The analyte nucleic acid and the one or more nucleic acid probes may interact to form an aggregate that may coat or cover at least part of the inner surface or the inner space of the channel, thereby enhancing an electrical pathway along the length of the channel. If the aggregate is electrically conductive, this may cause a measurable increase in an electrical current and/or electrical conductivity measured along at least a portion of the length of the channel, and a measurable decrease in an electrical resistivity measured along at least a portion of the length of the channel.

[0232] In certain embodiments, the electrodes used in the detection system may be metallic, for example, aluminum, manganese and platinum. In other embodiments, the electrodes used in the detection system may be non-metallic.

[0233] Exemplary techniques may introduce both the sample and all of the sensor compounds (e.g., one or more nucleic acid probes) into a channel in the detection system that is especially configured and dimensioned to allow nucleic acid detection. In certain embodiments, the channel may be configured so that its depth and/or its width are substantially equal to or lower than a diameter of the aggregate particle. Upon introduction of the sample and the sensor compounds into the channel, formation of the aggregate may indicate presence of a nucleic acid in the sample, while absence of the aggregate may indicate absence of the nucleic acid in the sample.

[0234] When flow of the fluid and/or flow of the charged particles in the fluid is uninhibited (for example, due to absence of an aggregate), the conductive particles or ions in the fluid may travel along at least a portion of the length of the channel along the y-axis from the input port toward the output port. The movement of the conductive particles or ions may result in a first or "reference" electrical property value or range of values (e.g., of an electrical current, conductivity, resistivity) being detected by a nucleic acid detection circuit along at least a portion of the length of the channel. In some embodiments, an equilibration circuit may periodically or continually monitor electrical property values during a time period until the values reach equilibrium. The equilibration circuit may then select one of the values as the reference electrical property value to avoid the influence of transient changes in the electrical property.

[0235] The term "reference" electrical property value may refer to a value or range of values of an electrical property of a channel prior to introduction of a sample and all

of the sensor compounds (e.g., one or more nucleic acid probes) into the channel. That is, the reference value is a value characterizing the channel prior to any interaction between the nucleic acid in the sample and all of the sensor compounds. In some cases, the reference value may be detected at a time period after introduction of a sensor compound into the channel but before introduction of the sample and additional sensor compounds into the channel. In some cases, the reference value may be detected at a time period after introduction of a sensor compound and the sample into the channel but before introduction of additional sensor compounds into the channel. In some cases, the reference value may be detected at a time period before introduction of the sample or the sensor compounds into the channel. In some cases, the reference value may be predetermined and stored on a non-transitory storage medium from which it may be accessed.

[0236] In some cases, formation of an electrically conductive aggregate in the channel (due to interactions between a nucleic acid of interest in the sample and one or more nucleic acid probes) may enhance the electrical pathway along at least a portion of the length of the channel. In this case, the nucleic acid detection circuit may detect a second electrical property value or range of values (e.g., of an electrical current, conductivity, resistivity) along at least a portion of the length of the channel. In some embodiments, the nucleic acid detection circuit may wait for a waiting or adjustment time period after introduction of the sample and all of the sensor compounds into the channel prior to detecting the second electrical property value. The waiting or adjustment time period allows an aggregate to form in the channel and for the aggregate formation to alter the electrical properties of the channel.

[0237] In some embodiments, the equilibration circuit may periodically or continually monitor electrical property values during a time period after the introduction of the sample and all of the sensor compounds until the values reach equilibrium. The equilibration circuit may then select one of the values as the second electrical property value to avoid the influence of transient changes in the electrical property.

[0238] The comparison circuit may compare the second electrical property value to the reference electrical property value. If it is determined that the difference between the second value and the reference value corresponds to a predetermined range of increase in current or conductivity (or decrease in resistivity), the nucleic acid detection circuit may

determine that an aggregate is present in the channel and that, therefore, the nucleic acid is present in the sample.

[0239] In certain other cases, when flow of the fluid in the channel and/or flow of the charged particles in the fluid is partially or completely blocked (for example, by formation of an aggregate), the conductive particles or ions in the fluid may be unable to freely travel along at least a portion of the length of the channel along the y-axis from the input port toward the output port. The hindered or stopped movement of the conductive particles or ions may result in a third electrical property value or range of values (e.g., of an electrical current, conductivity, resistivity) being detected by the nucleic acid detection circuit along at least a portion of the length of the channel. The third electrical property value may be detected in addition to or instead of the second electrical property value. In some embodiments, the nucleic acid detection circuit may wait for a waiting or adjustment time period after introduction of both the sample and all of the sensor compounds into the channel prior to detecting the third electrical property value. The waiting or adjustment time period allows an aggregate to form in the channel and for the aggregate formation to alter the electrical properties of the channel.

[0240] In some embodiments, the equilibration circuit may periodically or continually monitor electrical property values during a time period after the introduction of the sample and all of the sensor compounds until the values reach equilibrium. The equilibration circuit may then select one of the values as the third electrical property value to avoid the influence of transient changes in the electrical property.

[0241] The comparison circuit may compare the third electrical property value to the reference electrical property value. If it is determined that the difference between the third value and the reference value corresponds to a predetermined range of decrease in current or conductivity (or increase in resistivity), the nucleic acid detection circuit may determine that an aggregate is present in the channel and that, therefore, the nucleic acid is present in the sample.

[0242] In certain embodiments, prior to use of the detection system, the channel may be free of the sensor compounds (e.g., one or more nucleic acid probes). That is, a manufacturer of the detection system may not pre-treat or modify the channel to include the sensor compound. In this case, during use, a user may introduce one or more sensor

compounds, for example in an electrolyte buffer, into the channel and detect a reference electrical property value of the channel with the sensor compound but in the absence of a sample.

[0243] In certain other embodiments, prior to use of the detection system, the channel may be pre-treated or modified so that at least a portion of an inner surface of the channel includes or is coated with a sensor compound (e.g., one or more nucleic acid capture probes). In one example, the manufacturer may detect a reference electrical property value of the channel modified with the sensor compound and, during use, a user may use the stored reference electrical property value. That is, a manufacturer of the detection system may pre-treat or modify the channel to include a sensor compound. In this case, a user may need to introduce the sample and one or more additional sensor compounds into the channel.

[0244] In one example, the user may introduce one or more sensor compounds (e.g., one or more nucleic acid probes) and the sample into the channel concurrently, for example, in a mixture of the sensor compound and the sample. In this case, a reference electrical property value may be detected in the channel prior to introduction of the mixture, and an electrical property value may be detected after introduction of the mixture. Comparison of the electrical property value to the reference electrical property value may be used to determine if the nucleic acid is present in the sample.

[0245] In another example, the user may introduce one or more sensor compounds (e.g., one or more nucleic acid probes) and the sample into the channel concurrently, for example, in a mixture of the sensor compound and the sample. A stored reference electrical property value characterizing the channel prior to introduction of the mixture may be retrieved or accessed from a non-transitory storage medium. An electrical property value may be detected after introduction of the mixture into the channel. Comparison of the electrical property value to the stored reference electrical property value may be used to determine if the nucleic acid is present in the sample.

[0246] In another example, the user may first introduce one or more sensor compounds (e.g., one or more nucleic acid probes) into the channel, and detect a reference electrical property value prior to introduction of the sample into the channel. The user may subsequently introduce the sample and optionally, one or more additional sensor compounds, into the channel, and detect an electrical property value after waiting for a time period after

introduction of the sample into the channel. Comparison of the electrical property value to the reference electrical property value may be used to determine if the nucleic acid is present in the sample.

[0247] In another example, the user may first introduce one or more sensor compounds (e.g., one or more nucleic acid probes) into the channel, and may subsequently introduce the sample and optionally, one or more additional sensor compounds, into the channel. The user may then detect an electrical property value after waiting for a time period after introduction of the sample into the channel. A stored reference electrical property value characterizing the channel prior to introduction of the sample and all of the sensor compounds may be retrieved or accessed from a non-transitory storage medium. Comparison of the stored electrical property value to the reference electrical property value may be used to determine if the nucleic acid is present in the sample.

[0248] In another example, the user may first introduce the sample into the channel, and detect a reference electrical property value with only the sample in the channel. The user may subsequently introduce the sensor compounds (e.g., one or more nucleic acid probes) into the channel, and detect an electrical property value after waiting for a time period after introduction of the sensor compounds into the channel. Comparison of the electrical property value to the reference electrical property value may be used to determine if the nucleic acid is present in the sample.

[0249] In another example, the user may first introduce the sample into the channel, and may subsequently introduce the sensor compounds (e.g., one or more nucleic acid probes) into the channel. The user may then detect an electrical property value after waiting for a time period after introduction of the sensor compounds into the channel. A stored reference electrical property value characterizing the channel prior to introduction of the sample and all of the sensor compounds may be retrieved or accessed from a non-transitory storage medium. Comparison of the stored electrical property value to the reference electrical property value may be used to determine if the nucleic acid is present in the sample.

[0250] In certain other embodiments, prior to use of the detection system, the channel may be pre-treated or modified so that at least a portion of an inner surface of the channel includes or is coated with a first sensor compound (e.g., one or more nucleic acid

capture probes). That is, a manufacturer of the detection system may pre-treat or modify the channel to include the sensor compound. The manufacturer may detect a reference electrical property value of the channel with the first sensor compound and may store the reference electrical property value on a non-transitory storage medium. During use, the user may introduce the sample and one or more additional sensor compounds (e.g., one or more nucleic acid probes) into the channel and detect an electrical property value after waiting for a time period after introduction of the sample into the channel. The stored reference electrical property value may be accessed or retrieved from the storage medium. Comparison of the electrical property value to the reference electrical property value may be used to determine if the nucleic acid is present in the sample.

[0251] In another example, the user may detect a reference electrical property value of the channel with prior to introducing the sample into the channel. The user may subsequently introduce the sample into the channel and detect an electrical property value after waiting for a time period after introduction of the sample into the channel. Comparison of the electrical property value to the reference electrical property value may be used to determine if the nucleic acid is present in the sample.

[0252] Figures 19A and 19B are flowcharts of an exemplary method 1900 for detecting a nucleic acid or nucleotide in a sample.

[0253] In step 1902, at least a portion of an inner surface of a channel may be pre-treated or covalently modified so that it includes or is coated with a material that enables attachment of a nucleic acid probe. Exemplary materials may include, but are not limited to, a silane compound (e.g., tricholorsilane, triethoxysilane, alkylsilane, perfluoro silane), zwitterionic sultone, poly(6-9)ethylene glycol (Peg), perfluorooctyl, fluorescein, an aldehyde, a graphene compound, and the like. The covalent modification of the inner surface of the channel may prevent non-specific absorption of certain molecules. In one example, covalent modification of the inner surface may enable covalent bonding of one or more nucleic acid capture probes to the inner surface while preventing non-specific absorption of other molecules to the inner surface.

[0254] The channel modification material may be a silane compound in one example. The silane modification may be useful in attaching one or more probes, e.g., nucleic acid probes, to the inner surface of the channel. In one exemplary technique of

"silanizing" the inner surface, a solution is produced. The solution may be between 0.1% and 4% v/v (if silane is liquid) or w/v (if silane is a solid) of appropriate chloro-, trichloro-, trimethoxy- or triethoxysilane in the appropriate solvent (e.g. toluene for trimethoxy- or triethoxysilanes, ethanol for chloro- or trichlorosilanes or water with a pH between 3.5 to 5.5 for trimethoxysilanes). In one example, 1 mL of triethoxyeldehyde silane may be dissolved in 24 mL toluene, and the solution may be filtered through a 0.2 micron surfactant free cellulose acetate (SFCA) filter. 10 μL of the filtered silane solution may be added to a port of the channel and allowed to capillary fill the channel for 5 minutes. This may or may not be observed by light microscopy and may take between five and forty minutes depending upon the solvent composition. After capillary filling is complete, 10 μL of the filtered silane solution may be added to the remaining ports of the channel. The entire channel is immersed in the filtered silane solution and allowed to react for the desired amount of time (for example, 1 to 24 hours) at the desired temperature (for example, 20°C to 80°C depending upon the specific silane and solvent composition used for the modification). In one example, the channel may be immersed in the filtered silane solution and heated at 45°C for 18 hours. After the desired reaction time is over, the silanization process may be quenched using one of the following techniques. A catalytic amount of acetic acid may be added to toluene or ethanol-based surface modifications in some cases.

[0255] In one exemplary technique of quenching, the entire channel may be transferred to a container filled with 25 mL of 0.2 micron SFCA filtered ethanol, and stored until the desired time for use or further modification. In another exemplary technique of quenching, the channel may be electrokinetically washed with an appropriate solvent composition. In one electrokinetic washing technique for toluene modification of a channel, toluene is electrokinetically driven through the channel at a 10V to 1000V differential between electrodes for 5 to 15 minutes, followed by electrokinetically driving ethanol through the channel at a 10V to 1000V differential between electrodes for 5 to 15 minutes, followed by electrokinetically driving a 1:1 mixture of ethanol:water through the channel at 10V to 1000V differential between electrodes for 5 to 15 minutes, followed by a final electrokinetic driving of water through the channel at 10 V to 1000 V for 5 to 15 minutes. Proper operation of the channel may be confirmed by measuring the current at 1000 V applied field to an added 50 mM sodium borate buffer in the channel (giving a current

reading of approximately 330 nA) and re-addition of ultrapure (e.g., MilliQ ultrapure) water at the same applied field affording a current of less than 20 nA but greater than zero.

[0256] In step 1904, one or more nucleic acid probes (e.g., a capture probe) may be attached to at least a portion of the modified inner surface of the channel. In one embodiment, the nucleic acid probe may be covalently attached to the modified inner surface of the channel.

[0257] In one example of step 1904, the channel modified as in step 1902 may be placed on a hot plate at a low setting for 15 minutes to remove all ethanol from the channel. 2 μL of 1 mM stock 5' hydrazide modified DNA may be mixed with 198 μL of pH 4.5 buffer containing 50 mM sodium acetate and 1 mM 5-methoxyanthranilic acid. The final DNA concentration in the solution may be 10 μM. 20 μL of this solution may be added to a port of the modified channel and allowed to capillary fill the channel for 40 minutes. Subsequently, 10 μL of the solution may be added to the remaining ports of the channel. Loading of the solution in the channel may be ensured electrokinetically by connecting electrodes to the ports of the channel and maintaining a 700 V potential difference using a Kiethley 2410 device for 5 minutes or until a stable current is detected. In one example, a stable current of 230 nA may be detected. The solution may be allowed to remain in the channel to modify the channel for 3 hours. Subsequently, the channel may be electrokinetically washed with ultrapure (e.g., MilliQ ultrapure) water at a 1000 V potential difference between two ports until a current of less than 10 nA is detected. The modified channel may then be stored in a vacuum dessicator until use in the later steps.

[0258] In step 1906, a pre-mixture of a sample and a nucleic acid probe (e.g., a cross-linking target probe) may be prepared. In one example, the cross-linking target probe is selected so that it binds both with the capture probe provided at the inner surface of the channel in step 704 and with the analyte nucleic acid if it is present in the sample. In step 1908, the pre-mixture may be introduced into the channel. In one example, the sample may be a human liver total RNA extract (which may or may not include the analyte GAPD RNA). In this case, the pre-mixture may include a solution containing 45.5 μL nuclease-free water, 33.3 μL lysis buffer, 1 μL blocking reagent, 0.3 μL of a nucleic acid probe (e.g., a cross-linking target probe), and 20 μL of 20 ng/mL human liver total RNA extract that is vortex mixed. 10 μL of this solution may be introduced into the channel through one port and

allowed to capillary fill the channel. 10 μL of the same solution may then be introduced into another port of the channel.

[0259] In step 1910, a potential difference may be applied across at least a portion of the length of the channel using a voltage source. In step 1912, while the potential difference is being applied, one or more electrical property values (e.g., current, conductivity, resistivity) may be detected along at least a portion of the length of the channel. In one example, a potential difference of +1000 V may be applied, and an electrical current value of 0.4 μA may be detected.

[0260] In order to obtain an accurate and reliable measure of the electrical current, in step 1914, an equilibration circuit may be used to analyze a first set of two or more values of the values that were detected in step 1912. The equilibration circuit may determine if the values have reached equilibrium, i.e., have stopped temporally varying outside of a predetermined variance or tolerance range. If it is determined that the values have not reached equilibrium, then the method may return to step 1912 to detect additional values. On the other hand, if it is determined that the values have reached equilibrium, then the method may proceed to step 1916. In step 1916, the equilibration circuit may select a first or reference value from the first set of values. The first or reference value may be used to represent one or more electrical properties of the channel prior to formation of any aggregate particles in the channel.

[0261] In certain other examples, the first value may be measured when the channel is filled only with a wash buffer and/or only with a diluent buffer containing no nucleic acids. In one example, at a potential difference at +1000 V, the first electrical property value may be a current of 13-19 nA (for a wash buffer) and 380-400 nA (for a diluent buffer).

[0262] In step 1918, in some embodiments, the channel may be incubated and washed with a suitable wash buffer to remove nucleic acids that are not specifically bound into an aggregate in the channel. Optionally, an electrical property value may be detected subsequently. In step 1920, one or more additional nucleic acid probes may be introduced into the channel. Exemplary nucleic acid probes may include one or more label extenders selected so that they bind directly or indirectly with the analyte nucleic acid, and/or one or more amplification probes selected so that they bind with the label extenders. The

interactions result in the formation of an aggregate, which may be electrically conductive in some cases. The electrically conductive aggregate may enhance the electrical conductivity in the channel and may result in a measurable increase in an electrical property value (e.g., current, conductivity) and a measurable decrease in another electrical property value (e.g., resistivity) if the analyte nucleic acid is present in the sample.

[0263] In some cases in which multiple nucleic acid probes are sequentially introduced, steps 1918 and 1920 may be repeated for the introduction of each nucleic acid probe.

[0264] In step 1922, in some embodiments, the channel may be incubated and washed with a suitable wash buffer to remove nucleic acids that are not specifically bound into an aggregate formation in the channel. In one example, the channel may be sealed and incubated at 50°C for 90 minutes, and then allowed to cool to room temperature for 45 minutes. The channel may then be cleaned with a wash buffer until a stable current is detected.

[0265] In step 1924, a potential difference may be applied across at least a portion of the length of the channel using a voltage source. In step 1926, while the potential difference is being applied, one or more electrical property values along at least a portion of the length of the channel may be detected.

[0266] In order to obtain an accurate and reliable measure of the electrical current, in step 1928, an equilibration circuit may be used to analyze a second set of two or more values that were detected in step 1926. The equilibration module may determine if the values have reached equilibrium, i.e., have stopped temporally varying outside of a predetermined variance or tolerance range. If it is determined that the values have not reached equilibrium, then the method may return to step 1926 to detect additional values. On the other hand, if it is determined that the values have reached equilibrium, the method may proceed to step 1930.

[0267] In step 1930, the equilibration circuit may select a second value from the second set of values. The second value may be used to represent one or more electrical properties of the channel after any interaction between the nucleic acid and all of the nucleic acid probes. In one example, at a potential difference of +10 V, a current of 1 μA to 3.5 μA

may be detected if the sample contains the nucleic acid. At a potential difference of +100 V, a current of 3 μA to 20 μA may be detected if the sample contains the nucleic acid.

[0268] In step 1932, the comparison circuit may be used to determine a difference between the first or reference value (determined in step 1916) and the second value (determined in step 1930). In step 1934, the comparison circuit may determine if the difference determined in step 1932 satisfies a predetermined threshold, for example, if the difference is above a predetermined value, below a predetermined value, or if the difference is within a predetermined range. In one example in which the aggregate is electrically conductive, the second electrical property value may be 1 μA to 20 μA greater than the first or reference value, a range of values that indicates formation of an aggregate in the channel that is electrically conductive and that enhances the electrical conductivity of the channel, thereby indicating that the sample included the nucleic acid. In another example, the second electrical property value may be 1 μA to 20 μA lower than the first or reference value, a range of values that indicates formation of an aggregate in the channel, thereby indicating that the sample included the nucleic acid.

[0269] If it is determined in step 1934 that the difference between the first and second values satisfies the predetermined threshold, then the nucleic acid detection circuit may determine in step 1940 that the sample contains the nucleic acid. Subsequently, in step 1942, the nucleic acid detection circuit may store, on a non-transitory computer-readable medium, an indication that the sample contains the nucleic acid. Alternatively or additionally, in step 1942, the nucleic acid detection circuit may display, on a display device, an indication that the sample contains the nucleic acid.

[0270] On the other hand, if it is determined in step 1934 that the difference between the first and second values does not satisfy the predetermined threshold, then the nucleic acid detection circuit may determine in step 1936 that the sample does not contain the nucleic acid. Subsequently, in step 1938, the nucleic acid detection circuit may store, on a non-transitory computer-readable medium, an indication that the sample does not contain the nucleic acid. Alternatively or additionally, in step 1938, the nucleic acid detection circuit may display, on a display device, an indication that the sample does not contain the nucleic acid.

[0271] In one example of steps 1918-1932, the channel may be sealed and incubated in an oven at 55°C for 16 hours and then removed from the oven. 10 μL of a wash buffer may be electrokinetically driven through the channel for 10 minutes, a potential difference of +100 V may be applied, and an electrical property value may be detected. An exemplary electrical property value detected may be current ranging from 6 μA to 7.5 μA. Subsequently, 10 μL of a solution containing 1 μL of a nucleic acid probe (e.g., a pre-amplification probe) in 1 mL of diluent buffer may be electrokinetically driven into the channel. A potential difference of +100 V may be applied, and an electrical property value may be detected. An exemplary electrical property value detected may be current ranging from 5.8 μA to 7.5 μA.

[0272] The channel may then be sealed and incubated at 55°C for an hour. 10 μL of a wash buffer may be electrokinetically driven through the channel for 10 minutes, a potential difference of +100 V may be applied, and an electrical property value may be detected. An exemplary electrical property value detected may be current ranging from 2.8 μA to 3.2 μA. Subsequently, 10 μL of a solution containing 1 μL of a nucleic acid probe (e.g., an amplification probe) in 1 mL of diluent buffer may be electrokinetically driven into the channel until the current is detected to be stable. A potential difference of +100 V may be applied, and an electrical property value may be detected. An exemplary electrical property value detected may be current of 4 μA.

[0273] The channel may then be sealed and incubated at 55°C for an hour. 10 μL of a wash buffer may be electrokinetically driven through the channel for 10 minutes, a potential difference of +100 V may be applied, and an electrical property value may be detected. An exemplary electrical property value detected may be current ranging from 5 μA to 20 μA. Subsequently, 10 μL of a solution containing 1 μL of a nucleic acid probe (e.g., a label extender) in 1 mL of diluent buffer may be electrokinetically driven into the channel until the current is detected to be stable. A potential difference of +100 V may be applied, and an electrical property value may be detected. An exemplary electrical property value detected may be current ranging from 3 μA to 10 μA.

[0274] In certain embodiments, the channel may be reused for subsequent testing of samples. In one exemplary embodiment, in step 1946, a de-aggregation agent (e.g., a nucleic acid surface cleavage or degradation buffer) may be introduced into the channel to

cause the aggregate to disintegrate so that the channel may be reused. In step 1948, the channel may be filled with an electrolyte buffer to flush out the aggregate from the channel and one or more electrical properties (e.g., current) may be detected to ensure that the aggregate has been cleared from the channel. In one example, a marked reduction in the electrical current may indicate that an electrically conductive aggregate has been cleared from the channel.

[0275] In one example of steps 1946 and 1948, the channel with the aggregate is electrokinetically loaded with a buffer containing 50 mM sodium phosphates (pH 7.4), 1 mM 5-methoxyanthranilic acid and 5 mM hydroxylamine hydrochloride until a stable current is obtained (+/- 100 V = 1.4 – 1.7 μA). The entire channel is then allowed to incubate in this buffer for 18 hours at room temperature, after which the current is again measured until stable (+ 1000 V = 86 – 87 nA, -1000 V = 63 – 64 nA). The significant decrease in current (from 1.4-1.7 μA before introduction of the surface cleavage buffer to 63-90 nA after washing with the surface cleavage buffer) is indicative of clearing of the electrically conductive aggregate.

[0276] In certain embodiments, in step 1944, prior to disintegration of the aggregate, an absolute or relative concentration of a nucleic acid may be determined based on an electrical property value of the channel. The concentration of the nucleic acid may be determined in such a manner because the channels of exemplary detection systems have a high inner surface area to volume ratio. At low concentrations of the nucleic acid, electrical conductivity in the channel is dominated by surface charges. As such, measurements of electrical properties of the channel can enable distinction between different ions. As a result, unique and sensitive measurements of the bulk flow in the channel can be used to determine information on the surface charges at the inner surface of the channel. Exemplary embodiments may thus compute predetermined ranges of electrical property values of the channel that are characteristic of the nucleic acid particles given the dimensions of the channel and at different concentrations of the nucleic acid. These predetermined values may then be used to determine an unknown concentration of the nucleic acid in a sample.

[0277] Detailed information on surface charges in the channel for different ions is presented in the following papers, the entire contents of which are expressly incorporated herein by reference: “Surface-dependent chemical equilibrium constants and capacitances for

bare and 3-cyanopropyldimethylchlorosilane coated silica nanochannels," M. B. Andersen, J. Frey, S. Pennathur and H. Bruus, J., Colloid Interface Sci. 353, 301-310 (2011), and "Hydronium-domination ion transport in carbon-dioxide-saturated electrolytes at low salt concentrations in nanochannels," K.L. Jensen, J.T. Kristensen, A.M. Crumrine, M.B.Andersen, H. Bruus and S. Pennathur, Phys. Review E. 83, 5, 056307.

[0278] Figure 5 is a schematic drawing of the inside of a channel including an inner surface of the channel 502, an immobile layer of fluid 504 lying immediately adjacent to the inner surface of the channel, a diffusive layer of fluid 506 lying immediately adjacent to the immobile layer, and a bulk fluid flow layer 508 lying immediately adjacent to the diffusive layer. Exemplary ions are represented in each of the fluid layers. Upon application of a potential difference across the length of the channel, an electrical property value may be detected along at least a portion of the channel (for example, by the analyte detection circuit 122). The comparison circuit 124 may be used to compare the measured electrical property value to a predetermined range of electrical property values that correspond to a particular concentration or range of concentration values of the nucleic acid. The concentration determined may be an absolute concentration of the nucleic acid or a relative concentration of the nucleic acid with respect to the concentrations of one or more other substances in the channel.

[0279] Figures 6A and 6B are graphs showing conductivity values measured in a channel for different test cases. In each test case, a different relative concentration of an analyte relative to concentrations of two additional substances (in this case, ammonium and hydrogen peroxide) is used, and the corresponding conductivity value is determined in the channel. In one embodiment, Standard Clean 1 or SC1 is used a solution in the test cases. Details of SC1 can be found online. The ratios of concentrations among the three substances in the test cases represented in Figures 6A and 6B are presented in Table 1 above.

[0280] The lower the concentration of an analyte, the easier it is to measure differences in relative concentrations between the analyte and other substances. For example, at concentration ratios of 1000:1:1, detection sensitivity on the order of 1-10 ppm may be achieved in the exemplary detection system. At concentration ratios of 350:1:1, detection sensitivity on the order of 100 ppm may be achieved. At concentration ratios of 5:1:1, detection sensitivity on the order of 10,000 ppm may be achieved.

[0281] TABLE 3 summarizes exemplary electrical current values that may be detected at different stages of the method of Figures 19A and 19B. One of ordinary skill in the art will recognize that the exemplary numerical values presented in TABLE 3 are merely for illustrative purposes and are not intended to limit the scope of the invention.

TABLE 3

Step	**Applied Voltage**	**Measured Current**
Introduction of sample and capture components (step 708)	+ 1000V - 1000V	409 – 410 nA 403 – 404 nA
Wash of sample and capture components after 16 hr incubation at 55 °C (Step 716)	+/- 100V	6 – 7.5 μA
Loading of preamplifier probes (Step 720)	+/- 100V	5.8 – 7.5 μA
Washing of preamplifier probes after 1 hr incubation at 55 °C (Step 718)	+/- 100V	2.8 – 3.2 μA
Loading of amplifier probes (Step 720)	+/- 100V	4 μA
Washing of amplifier probes after 1 hr incubation at 55 °C(Step 718)	+/- 100V	5 – 20 μA
Loading of label probes (Step 720)	+ 100V - 100V	30 μA 3 – 10 μA
Washing of label probes after incubation (Step 718)	+10 V - 10 V	0.9 – 1.4 μA 2 – 3.5 μA
Loading of surface cleavage/degradation buffer (Step 746)	+/- 100V	1.4 – 1.7 μA
Washing of surface cleavage buffer (Step 748)	+ 1000V - 1000V	86 – 87 nA 63 – 64 nA

[0282] In one example, one or more electrical properties of a channel with no surface modification were detected in which only buffers with no added nucleic acids were exposed to the channel. TABLE 4 summarizes the stable currents that were detected when a wash buffer and a diluent buffer were present in the channel.

TABLE 4

Buffer	**Applied Voltage**	**Measured Current**
Wash buffer	+ 1000V - 1000V	19 nA 13 nA
Diluent buffer	+ 1000V - 1000V	396 nA 385 nA

[0283] Figure 20 is a flowchart illustrating a general exemplary method 2000 for detecting the presence or absence of a nucleic acid in a sample. In step 2002, a sample may be introduced into a channel of a detection system, the channel having a length and a width, the length substantially greater than the width. In step 2004, an electrical property value of an electrical property (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of the channel after the sample is introduced into the channel. In step 2006, a reference electrical property value may be accessed. The reference electrical property value may be associated with the electrical property detected in step 2004 along at least a portion of the length of the channel prior to introduction of the sample into the channel. In step 2008, the electrical property value measured in step 2004 may be compared to the reference electrical property value accessed in step 2006. In step 2010, based on the comparison in step 2008, presence or absence of the nucleic acid in the sample may be determined.

[0284] Figure 21 is a flowchart illustrating a general exemplary method 2100 for detecting the presence or absence of a nucleic acid in a sample. In step 2102, one or more electrical property values of one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of a channel, the channel having a length and a width, the length substantially greater than the width. In step 2104, a reference channel electrical property value may be determined based on the electrical property values of the channel measured in step 2102. In step 2106, a sample may be introduced into the channel. In step 2108, one or more electrical property values of one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of the channel after introduction of the sample into the channel. In step 2110, a sample channel electrical property value may be determined based on the one or more electrical property values measured in step 2108. In step 2112, the sample channel electrical property value determined in step 2110 may be compared to the reference channel electrical property value determined in step 2104. In step 2114, based on the comparison in step 2112, presence or absence of the nucleic acid in the sample may be determined.

[0285] Figure 22 is a flowchart illustrating a general exemplary method 2200 for detecting the presence or absence of a nucleic acid in a sample. In step 2202, a mixture of a

sample and one or more sensor compounds may be introduced into a channel, the channel having a length and a width, the length substantially greater than the width. In step 2204, an electrical property value of an electrical property (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of the channel after the sample and all of the sensor compounds are introduced into the channel. In step 2206, a reference electrical property value may be accessed. The reference electrical property value may be associated with the electrical property detected in step 2204 along at least a portion of the length of the channel prior to introduction of the sample and all of the sensor compounds into the channel. In step 2208, any differences between the electrical property value measured in step 2204 and the reference electrical property value accessed in step 2206 may be determined. In step 2210, based on the differences, if any, determined in step 2208, presence or absence of the nucleic acid in the sample may be determined.

[0286] Figure 23 is a flowchart illustrating a general exemplary method 2300 for detecting the presence or absence of a nucleic acid in a sample. In step 2302, one or more sensor compounds may be introduced into a channel, the channel having a length and a width, the length substantially greater than the width. In step 2304, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of a channel. In step 2306, a reference channel electrical property value may be determined based on the electrical properties of the channel measured in step 2304. In step 2308, a sample may be introduced into the channel. In step 2310, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of a channel. In step 2312, an electrical property value of the channel may be determined based on the one or more electrical properties measured in step 2310. In step 2314, any differences between the electrical property value determined in step 2312 and the reference channel electrical property value determined in step 2306 may be determined. In step 2316, based on the differences, if any, determined in step 2314, presence or absence of the nucleic acid in the sample may be determined.

[0287] Figure 24 is a flowchart illustrating a general exemplary method 2400 for detecting the presence or absence of a nucleic acid in a sample. In step 2402, one or more sensor compounds may be introduced into a channel, the channel having a length and a width, the length substantially greater than the width. In step 2404, a sample may be

introduced into the channel. In step 2406, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of a channel. In step 2408, an electrical property value of the channel may be determined based on the one or more electrical properties measured in step 2406. In step 2410, a reference channel electrical property value may be accessed. The reference channel electrical property value may be measured prior to introduction of all of the sensor compounds and the sample into the channel. In step 2412, any differences between the electrical property value determined in step 2408 and the reference channel electrical property value accessed in step 2410 may be determined. In step 2414, based on the differences, if any, determined in step 2412, presence or absence of the nucleic acid in the sample may be determined.

[0288] Figure 25 is a flowchart illustrating a general exemplary method 2500 for detecting the presence or absence of a nucleic acid in a sample. In step 2502, a sample may be introduced into a channel of a detection system, the channel having a length and a width, the length substantially greater than the width. In step 2504, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of the channel after the sample is introduced into the channel. In step 2506, a reference channel electrical property value may be determined based on the one or more electrical properties measured in step 2504. In step 2508, one or more sensor compounds may be introduced into the channel. In step 2510, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of the channel after the sensor compounds are introduced into the channel. In step 2512, an electrical property value may be determined based on the one or more electrical properties measured in step 2510 after all of the sensor compounds and the sample are introduced into the channel. In step 2514, any differences between the electrical property value determined in step 2512 and the reference channel electrical property value determined in step 2506 may be determined. In step 2516, based on the differences, if any, determined in step 2514, presence or absence of the nucleic acid in the sample may be determined.

[0289] Figure 26 is a flowchart illustrating a general exemplary method 2600 for detecting the presence or absence of a nucleic acid in a sample. In step 2602, a sample may be introduced into a channel of a detection system, the channel having a length and a width, the length substantially greater than the width. In step 2604, one or more sensor compounds

may be introduced into the channel. In step 2606, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of the channel after the sample and all of the sensor compounds are introduced into the channel. In step 2608, an electrical property value may be determined based on the one or more electrical properties measured in step 2606 after all of the sensor compounds and the sample are introduced into the channel. In step 2610, a reference channel electrical property value may be accessed. The reference channel electrical property value may be measured prior to introduction of all of the sensor compounds and the sample into the channel. In step 2612, any differences between the electrical property value determined in step 2608 and the reference channel electrical property value accessed in step 2610 may be determined. In step 2614, based on the differences, if any, determined in step 2612, presence or absence of the nucleic acid in the sample may be determined.

[0290] Figure 27 is a flowchart illustrating a general exemplary method 2700 for detecting the presence or absence of a nucleic acid in a sample. In step 2702, at least a portion of an inner surface of a channel may be modified or treated with a material that may facilitate or enable specific covalent attachment of one or more nucleic acid probes to the inner surface of the channel. The channel may have a length and a width, the length substantially greater than the width. Exemplary materials that may be used to modify the inner surface of the channel include, but are not limited to, a silane compound (e.g., tricholorsilane, alkylsilane, triethoxysilane, perfluoro silane), zwitterionic sultone, poly(6-9)ethylene glycol (Peg), perfluorooctyl, fluorescein, an aldehyde, a graphene compound, and the like. The covalent modification of the inner surface of the channel may prevent non-specific absorption of certain molecules, for example, molecules other than nucleic acid probes. In step 2704, at least a portion of the inner surface of the channel may be coated or provided with one or more nucleic acid probes. The nucleic acid probes may be covalently attached to the modified portion of the inner surface. In step 2706, one or more electrical properties (e.g., current, conductivity, resistance) may be measured along at least a portion of the length of a channel. In step 2708, a reference channel electrical property value may be determined based on the one or more electrical properties measured in step 2706. In step 2710, the reference channel electrical property value may be stored on a non-transitory

storage medium for use in determining whether a nucleic acid is present or absent in the sample.

[0291] Figure 28 is a schematic of exemplary nucleic acid probes that may be used in the methods of Figures 19A, 19B, 20-27, 29A and 29B. Figure 28 illustrates an inner surface 2802 of a channel 2804 which is pre-treated or modified (for example, with molecules of a silane compound) to enable attachment of one or more nucleic acid probes (e.g., capture probes 2806) to the inner surface 2802. The capture probes 2806 are selected so that they bind with one or more cross-linking target probes 2808, and the target probes 2808 are selected so that they bind both with a particular nucleic acid 2810 (which is the analyte being tested for, and which may be a viral DNA in one example) and the capture probes 2806.

[0292] A sample (which may or may not contain the nucleic acid 2810) and the target probes 2808 may be introduced into the channel concurrently or sequentially. Interactions among the nucleic acid 2810, the target probes 2808 and the capture probes 2806 may result in an aggregate 2812 in the channel. In certain embodiments, one or more additional nucleic acid probes (e.g., one or more label extenders 2814) may be introduced into the channel. The label extenders 2814 are selected so that they bind with the nucleic acid 2810 in the aggregate 2812 to form a more complex aggregate 2816. One or more additional nucleic acid probes (e.g., one or more amplification probes 2818) may also be introduced into the channel. The amplification probes 2818 are selected so that they bind with the label extenders 2814 in the aggregate 2816 to form a more complex aggregate 2820 that may be electrically conductive in some cases. The electrically conductive aggregate 2820 may enhance the electrical pathway along at least a portion of the length of the channel, and may result in a measurable increase in an electrical property value (e.g., current, conductivity) and a measurable decrease in another electrical property value (e.g., resistivity) compared to a reference value, if the nucleic acid is present in the sample. Thus, detection of an increased electrical current or conductivity in the channel, relative to a reference value, may indicate the presence of the nucleic acid 2810 in a sample. Similarly, detection of a decreased resistivity relative to a reference value may indicate the presence of the nucleic acid 2810 in a sample.

[0293] Another exemplary technique for detecting a nucleic acid may involve detection of the presence of a diode-like behavior in the channel that is caused by the formation of a nucleic acid aggregate in the channel. In the absence of an aggregate, application of a potential difference having a substantially similar magnitude (e.g., +500 V) may result in a substantially same magnitude of an electrical property (e.g., current) detected along the length of the channel regardless of the direction of application of the potential difference or electric field. If the potential difference is applied across the length of the channel in a first direction along the length of the channel (e.g., such that the positive electrode is at an input port 110 at or near a first end of the channel and such that the negative electrode is at an output port 112 at or near a second end of the channel), the resulting current may be substantially equal in magnitude to the resultant current if the potential difference is applied in the opposite direction (e.g., such that the positive electrode is at the output port 112 and such that the negative electrode is at the input port 110).

[0294] Formation of an aggregate in the channel may cause a diode-like behavior in which reversal of the direction of the applied potential difference or electric field causes a change in the electrical property detected in the channel. The diode-like behavior causes the detected electrical current to vary in magnitude with the direction of the electric field. When the electric field or potential difference is applied in the first direction, the magnitude of the electrical current may be different in magnitude than when the potential different or electric field is applied in the opposite direction. Thus, comparison between a first electrical property value (detected when a potential difference is applied in a first direction along the channel length) and a second electrical property value (detected when a potential difference is applied in a second opposite direction along the channel length) may enable detection of an aggregate, and thereby detection of a nucleic acid in the sample. If the first and second electrical property values are substantially equal in magnitude, then it may be determined that the sample does not contain the nucleic acid. On the other hand, if the first and second electrical property values are substantially unequal in magnitude, then it may be determined that the sample contains the nucleic acid. In other words, the sum of the values of the electrical property (positive in one direction, negative in the other direction) is substantially zero in the absence of an aggregate and substantially non-zero in the presence of an aggregate.

[0295] Figures 29A and 29B are flowcharts illustrating an exemplary method 2950 for detecting the presence or absence of the nucleic acid in a sample. In step 2952, one or more nucleic acid probes and a sample may be introduced into the channel using any suitable technique, for example, capillary filing or electro-kinetic filling. The nucleic acid probes and the sample may be introduced concurrently or separately. In one embodiment, at least a portion of an inner surface of the channel may be treated to include or be coated with a nucleic acid probe (e.g., a capture probe).

[0296] In step 2954, a potential difference may be applied across at least a portion of the length of the channel using a voltage source in a first direction along the channel length (y-axis). In step 2956, while the potential difference is being applied, one or more electrical properties values (e.g., the electrical current and/or conductivity) along at least a portion of the length of the channel may be detected. In some cases, the electrical current and/or conductivity may be directly measured. In other cases, a measure indicating the electrical current and/or a measure indicating the electrical conductivity may be detected.

[0297] In order to obtain an accurate and reliable measure of the electrical properties, in step 2958, a first set of two or more values that were detected in step 2956 may be continually or periodically monitored. It may be determined if the electrical property values have reached equilibrium, i.e., has stopped varying outside of a predetermined variance or tolerance range. If it is determined that the electrical property values have not reached equilibrium, then the method may return to step 2956 to detect additional electrical property values. On the other hand, if it is determined that the electrical property values have reached equilibrium, then the method may proceed to step 2960.

[0298] In step 1860, a first value may be selected from the first set of electrical property. The first electrical property value may be used to represent the one or more electrical properties (e.g., electrical current or conductivity) of the channel when an electric field is applied in a first direction along the channel length (y-axis).

[0299] In step 2962, a potential difference may be applied across at least a portion of the length of the channel using a voltage source in a second opposite direction along the channel length (y-axis). The second direction may be substantially opposite to the first direction. In step 2964, while the potential difference is being applied, one or more electrical properties (e.g., electrical current and/or conductivity) along at least a portion of the length of

the channel may be detected. In some cases, the electrical current and/or conductivity may be directly measured. In other cases, a measure indicating the electrical current and/or a measure indicating the electrical conductivity may be detected.

[0300] In order to obtain an accurate and reliable measure of the electrical properties, in step 2966, a second set of two or more values that were detected in step 2964 may be continually or periodically monitored. It may be determined if the electrical property values have reached equilibrium, e.g., has stopped temporally varying outside of a predetermined variance or tolerance range. If it is determined that the electrical property values have not reached equilibrium, then the method may return to step 2964 to detect additional values. On the other hand, if it is determined that the electrical property values have reached equilibrium, then the method may proceed to step 2968. In step 2968, a second value may be selected from the second set of values of the electrical property. The second value may be used to represent the one or more electrical properties (e.g., electrical current or conductivity) along at least a portion of the length of the channel after both the sample and the sensor compound have been introduced into the channel.

[0301] In step 2970, a difference between the magnitude of the first value (determined in step 2960) and the magnitude of the second value (determined in step 2968) may be determined. In step 2972, it may be determined if the difference determined in step 2970 satisfies a predetermined threshold, for example, if the difference is above a predetermined value, below a predetermined value, or if the difference is within a predetermined range.

[0302] If it is determined in step 2972 that the difference between the first and second values satisfies the predetermined threshold (e.g., that the difference in magnitudes is substantially non-zero), then it may be determined in step 2978 that the sample contains the nucleic acid. Subsequently, in step 2980, an indication that the sample contains the nucleic acid may be stored on a non-transitory storage medium. Alternatively or additionally, in step 2980, an indication that the sample contains the nucleic acid may be displayed on a display device.

[0303] On the other hand, if it is determined in step 2972 that the difference between the first and second values does not satisfy the predetermined threshold (e.g., that the difference in magnitudes is substantially zero), then it may be determined in step 2974

that the sample does not contain the nucleic acid. Subsequently, in step 2976, an indication that the sample does not contain the nucleic acid may be stored on a non-transitory storage medium. Alternatively or additionally, in step 2976, an indication that the sample does not contain the nucleic acid may be displayed on a display device.

[0304] In certain cases, if the difference in magnitude between the first and second values is greater than the threshold, then it may be determined that the sample contains the nucleic acid. Otherwise, it may be determined that the sample does not contain the nucleic acid. In certain non-limiting examples, the threshold may range from approximately 1 nA to approximately 10 nA.

[0305] In certain embodiments, the channel may be prepared for reuse for subsequent testing of samples. In step 2984, a de-aggregation agent may be introduced into the channel using any suitable technique, for example, capillary filing or electro-kinetic filling. The de-aggregation agent may be selected so that interaction between the de-aggregation agent and the aggregate formed in the channel causes the aggregate to dissolve or disintegrate. The channel may be filled with an electrolyte buffer to flush out the channel and allow a sample and a sensor compound to be introduced into the channel.

[0306] In certain embodiments, in step 2982, prior to disintegration of the aggregate, an absolute or relative concentration of the nucleic acid may be determined based on an electrical property value of the channel. The concentration of the nucleic acid may be determined in such a manner because the channels of exemplary detection systems have a high inner surface area to volume ratio. At low concentrations of the nucleic acid, electrical conductivity in the channel is dominated by surface charges. As such, measurements of electrical properties of the channel can enable distinction between different ions. As a result, unique and sensitive measurements of the bulk flow in the channel can be used to determine information on the surface charges at the inner surface of the channel. Exemplary embodiments may thus compute predetermined ranges of electrical property values of the channel that are characteristic of the nucleic acid given the dimensions of the channel and at different concentrations of the nucleic acid. These predetermined values may then be used to determine an unknown concentration of the nucleic acid in a sample.

VI. Exemplary processors and computing devices

[0307] Systems and methods disclosed herein may include one or more programmable processors, processing units and computing devices having associated therewith executable computer-executable instructions held or encoded on one or more non-transitory computer readable media, RAM, ROM, hard drive, and/or hardware. In exemplary embodiments, the hardware, firmware and/or executable code may be provided, for example, as upgrade module(s) for use in conjunction with existing infrastructure (for example, existing devices/processing units). Hardware may, for example, include components and/or logic circuitry for executing the embodiments taught herein as a computing process.

[0308] Displays and/or other feedback means may also be included, for example, for rendering a graphical user interface, according to the present disclosure. The displays and/or other feedback means may be stand-alone equipment or may be included as one or more components/modules of the processing unit(s).

[0309] The actual computer-executable code or control hardware that may be used to implement some of the present embodiments is not intended to limit the scope of such embodiments. For example, certain aspects of the embodiments described herein may be implemented in code using any suitable programming language type such as, for example, the MATLAB technical computing language, the LABVIEW graphical programming language, assembly code, C, C# or C++ using, for example, conventional or object-oriented programming techniques. Such computer-executable code may be stored or held on any type of suitable non-transitory computer-readable medium or media, such as, a magnetic or optical storage medium.

[0310] As used herein, a "processor," "processing unit," "computer" or "computer system" may be, for example, a wireless or wire line variety of a microcomputer, minicomputer, server, mainframe, laptop, personal data assistant (PDA), wireless e-mail device (for example, "BlackBerry," "Android" or "Apple," trade-designated devices), cellular phone, pager, processor, fax machine, scanner, or any other programmable device configured to transmit and receive data over a network. Computer systems disclosed herein may include memory for storing certain software applications used in obtaining, processing and communicating data. It can be appreciated that such memory may be internal or external to the disclosed embodiments. The memory may also include a non-transitory storage

medium for storing computer-executable instructions or code, including a hard disk, an optical disk, floppy disk, ROM (read only memory), RAM (random access memory), PROM (programmable ROM), EEPROM (electrically erasable PROM), flash memory storage devices, or the like.

[0311] Figure 18 depicts a block diagram representing an exemplary computing device 1700 that may be used to implement the systems and methods disclosed herein. In certain embodiments, the processor 130 illustrated in Figures 1A and 1B may be configured as or may implement certain functionality and/or components of the computing device 1700. In certain embodiments, the analyte detection circuit 122 may be configured as or may implement certain functionality and/or components of the computing device 1700.

[0312] The computing device 1700 may be any computer system, such as a workstation, desktop computer, server, laptop, handheld computer, tablet computer (e.g., the iPadTM tablet computer), mobile computing or communication device (e.g., the iPhoneTM mobile communication device, the AndroidTM mobile communication device, and the like), or other form of computing or telecommunications device that is capable of communication and that has sufficient processor power and memory capacity to perform the operations described herein. In exemplary embodiments, a distributed computational system may include a plurality of such computing devices.

[0313] The computing device 1700 may include one or more non-transitory computer-readable media having encoded thereon one or more computer-executable instructions or software for implementing the exemplary methods described herein. The non-transitory computer-readable media may include, but are not limited to, one or more types of hardware memory and other tangible media (for example, one or more magnetic storage disks, one or more optical disks, one or more USB flash drives), and the like. For example, memory 1706 included in the computing device 1700 may store computer-readable and computer-executable instructions or software for implementing functionality of an analyte detection circuit 122 as described herein. The computing device 1700 may also include processor 1702 and associated core 1704, and in some embodiments, one or more additional processor(s) 1702' and associated core(s) 1704' (for example, in the case of computer systems having multiple processors/cores), for executing computer-readable and computer-executable instructions or software stored in the memory 1702 and other programs for

controlling system hardware. Processor 1702 and processor(s) 1702' may each be a single core processor or a multiple core (1704 and 1704') processor.

[0314] Virtualization may be employed in the computing device 1700 so that infrastructure and resources in the computing device may be shared dynamically. A virtual machine 1714 may be provided to handle a process running on multiple processors so that the process appears to be using only one computing resource rather than multiple computing resources. Multiple virtual machines may also be used with one processor.

[0315] Memory 1706 may include a non-transitory computer system memory or random access memory, such as DRAM, SRAM, EDO RAM, and the like. Memory 1706 may include other types of memory as well, or combinations thereof.

[0316] A user may interact with the computing device 1700 through a visual display device 1718, such as a screen or monitor, which may display one or more graphical user interfaces 1720 provided in accordance with exemplary embodiments described herein. The visual display device 1718 may also display other aspects, elements and/or information or data associated with exemplary embodiments. In certain cases, the visual display device 1718 may display value of one or more electrical properties detected in an exemplary analyte detection system or method. In certain cases, the visual display device 1718 may display an indication of whether a sample contains or does not contain an analyte of interest. In certain embodiments, other types of interfaces may be provided to communicate the same information, for example, a sound alarm that may be activated if an analyte of interest is determined to be present in a sample.

[0317] The computing device 1700 may include other I/O devices for receiving input from a user, for example, a keyboard or any suitable multi-point touch interface 1708 or pointing device 1710 (e.g., a mouse, a user's finger interfacing directly with a display device). As used herein, a "pointing device" is any suitable input interface, specifically, a human interface device, that allows a user to input spatial data to a computing system or device. In an exemplary embodiment, the pointing device may allow a user to provide input to the computer using physical gestures, for example, pointing, clicking, dragging, dropping, and the like. Exemplary pointing devices may include, but are not limited to, a mouse, a touchpad, a finger of the user interfacing directly with a display device, and the like.

[0318] The keyboard 1708 and the pointing device 1710 may be coupled to the visual display device 1718. The computing device 1700 may include other suitable conventional I/O peripherals. The I/O devices may facilitate implementation of the one or more graphical user interfaces 1720, for example, implement one or more of the graphical user interfaces described herein.

[0319] The computing device 1700 may include one or more storage devices 1724, such as a durable disk storage (which may include any suitable optical or magnetic durable storage device, e.g., RAM, ROM, Flash, USB drive, or other semiconductor-based storage medium), a hard-drive, CD-ROM, or other computer readable media, for storing data and computer-readable instructions and/or software that implement exemplary embodiments as taught herein. In exemplary embodiments, the one or more storage devices 1724 may provide storage for data that may be generated by the systems and methods of the present disclosure. The one or more storage devices 1724 may be provided on the computing device 1700 and/or provided separately or remotely from the computing device 1700.

[0320] The computing device 1700 may include a network interface 1712 configured to interface via one or more network devices 1722 with one or more networks, for example, Local Area Network (LAN), Wide Area Network (WAN) or the Internet through a variety of connections including, but not limited to, standard telephone lines, LAN or WAN links (for example, 802.11, T1, T3, 56kb, X.25), broadband connections (for example, ISDN, Frame Relay, ATM), wireless connections, controller area network (CAN), or some combination of any or all of the above. The network interface 1712 may include a built-in network adapter, network interface card, PCMCIA network card, card bus network adapter, wireless network adapter, USB network adapter, modem or any other device suitable for interfacing the computing device 1700 to any type of network capable of communication and performing the operations described herein. The network device 1722 may include one or more suitable devices for receiving and transmitting communications over the network including, but not limited to, one or more receivers, one or more transmitters, one or more transceivers, one or more antennae, and the like.

[0321] The computing device 1700 may run any operating system 1716, such as any of the versions of the Microsoft® Windows® operating systems, the different releases of the Unix and Linux operating systems, any version of the MacOS® for Macintosh

computers, any embedded operating system, any real-time operating system, any open source operating system, any proprietary operating system, any operating systems for mobile computing devices, or any other operating system capable of running on the computing device and performing the operations described herein. In exemplary embodiments, the operating system 1716 may be run in native mode or emulated mode. In an exemplary embodiment, the operating system 1716 may be run on one or more cloud machine instances.

[0322] One of ordinary skill in the art will recognize that exemplary computing device 1700 may include more or fewer modules than those shown in Figure 18.

[0323] In describing exemplary embodiments, specific terminology is used for the sake of clarity. For purposes of description, each specific term is intended to, at least, include all technical and functional equivalents that operate in a similar manner to accomplish a similar purpose. Additionally, in some instances where a particular exemplary embodiment includes a plurality of system elements or method steps, those elements or steps may be replaced with a single element or step. Likewise, a single element or step may be replaced with a plurality of elements or steps that serve the same purpose. Further, where parameters for various properties are specified herein for exemplary embodiments, those parameters may be adjusted up or down by 1/20th, 1/10th, 1/5th, 1/3rd, 1/2nd, and the like, or by rounded-off approximations thereof, unless otherwise specified. Moreover, while exemplary embodiments have been shown and described with references to particular embodiments thereof, those of ordinary skill in the art will understand that various substitutions and alterations in form and details may be made therein without departing from the scope of the invention. Further still, other aspects, functions and advantages are also within the scope of the invention.

[0324] Exemplary flowcharts are provided herein for illustrative purposes and are non-limiting examples of methods. One of ordinary skill in the art will recognize that exemplary methods may include more or fewer steps than those illustrated in the exemplary flowcharts, and that the steps in the exemplary flowcharts may be performed in a different order than shown.

[0325] Blocks of the block diagram and the flow chart illustrations support combinations of means for performing the specified functions, combinations of steps for performing the specified functions and program instruction means for performing the

specified functions. It will also be understood that some or all of the blocks/steps of the circuit diagram and process flowchart, and combinations of the blocks/steps in the circuit diagram and process flowcharts, can be implemented by special purpose hardware-based computer systems that perform the specified functions or steps, or combinations of special purpose hardware and computer instructions. Exemplary systems may include more or fewer modules than those illustrated in the exemplary block diagrams.

[0326] Many modifications, combinations and other embodiments of the inventions set forth herein will come to mind to one skilled in the art to which these embodiments of the invention pertain having the benefit of the teachings presented in the foregoing descriptions and the associated drawings. Therefore, it is to be understood that the embodiments of the invention are not to be limited to the specific embodiments disclosed and that modifications, combinations and other embodiments are intended to be included within the scope of the appended claims. Although specific terms are employed herein, they are used in a generic and descriptive sense only and not for purposes of limitation.

[0327] In this specification where reference has been made to patent specifications, other external documents, or other sources of information, this is generally for the purpose of providing a context for discussing the features of the invention. Unless specifically stated otherwise, reference to such external documents is not to be construed as an admission that such documents, or such sources of information, in any jurisdiction, are prior art, or form part of the common general knowledge in the art.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method for detecting the presence or absence of an analyte in a sample, the method comprising:

introducing a sample into a channel, the channel having a length and a width, the length substantially greater than the width;

introducing a solution comprising a dissolved sensor compound into the channel, wherein the sensor compound is allowed to flow along the length of the channel;

measuring an electrical property value of an electrical property along at least a portion of the length of the channel after the sample and sensor compound are introduced into the channel;

accessing a reference electrical property value, wherein the reference electrical property value of an electrical property of the channel along at least a portion of the length of the channel is obtained prior to introduction of the sample into the channel;

comparing the measured electrical property value and the reference electrical property value; and

determining whether an aggregate is present in an inner space of the channel based on the comparison between the measured electrical property value and the reference electrical property value, wherein the aggregate is formed in the inner space of the channel by an interaction between the analyte and the sensor compound, thereby determining whether the analyte is present in the channel.

2. The method of claim 1, further comprising:

prior to introducing the sample into the channel, measuring one or more electrical properties of the channel along at least the portion of the length of the channel; and

determining the reference electrical property value based on the one or more electrical properties of the channel measured during the previous measuring step.

3. The method of claim 1, further comprising a step selected from: waiting for an adjustment time period between introducing the sample into the

channel and measuring the electrical property value; and displaying, on a visual display device, an indication of whether the analyte is present in the sample.

4. The method of claim 1, further comprising: applying a potential difference across the length of the channel during detection of the measured electrical property value.

5. The method of claim 1, wherein the measured electrical property value corresponds to a value of an electrical current conducted along at least the portion of length of the channel or to an electrical conductivity along at least the portion of the length of the channel.

6. The method of claim 1, wherein the channel is configured to have a dimension selected from a length ranging from 10 nanometers to 10 centimeters, a width ranging from 1 nanometer to 50 microns, or a depth ranging from 1 nanometer to 1 micron.

7. The method of claim 1, further comprising:

monitoring a first set of one or more values of the electrical property in the channel during a first time period, and a second set of one or more values of the electrical property in the channel during a second time period;

selecting the reference electrical property value from the first set of values upon equilibration of the one or more values in the channel during the first time period; and

selecting the measured electrical property value from the second set of values upon equilibration of the one or more values in the channel during the second time period.

8. The method of claim 1, further comprising: determining, based on the measured electrical property value, a concentration of the analyte in the sample.

9. The method of claim 1, further comprising: preparing the channel for reuse by introducing a de-aggregation agent into the channel, the de-aggregation agent causing disintegration of the aggregate.

10. The method of any one of claims 1-9, wherein the analyte is selected from the group consisting of:

a nucleic acid, wherein the sensor compound is a nucleic acid probe;

a silver ion, wherein the sensor compound is TPEA2; and

a mercury ion, wherein the sensor compound is TPET2.

11. A detection system for detecting an analyte in the presence of a sensor compound, comprising:

a substrate having at least one channel, wherein the at least one channel has a length and a width, wherein the length is substantially greater than the width, and comprises a solution comprising a dissolved sensor compound, wherein the sensor compound is allowed to flow along the length of the channel, and wherein an interaction between the analyte and the sensor compound results in formation of an aggregate;

a first port in fluid communication with a first end section of the at least one channel;

a second port in fluid communication with a second end section of the at least one channel;

a first electrode electrically connected at the first end section of the at least one channel and a second electrode electrically connected at the second end section of the at least one channel, the first and second electrodes electrically connected to their respective first and second end sections of the at least one channel to form a channel circuit, the channel circuit having electrical properties and configured such that when an electrically conductive fluid is present in the at least one channel, the electrically conductive fluid alters the electrical properties of the channel circuit; and

an analyte detection circuit in electrical communication with the first and second electrodes, the analyte detection circuit including a measurement circuit in electrical communication with the first and second electrode, the measurement circuit having a measurement circuit output, the measurement circuit output including one or more values indicative of one or more electrical properties of the channel circuit, the analyte detection circuit including a memory in electrical communication with the measurement circuit output and configured to store the one or more values indicative of the one or more electrical properties of the channel circuit including at least a first value of an electrical property of the channel circuit and a second value of the

electrical property of the channel circuit, the analyte detection circuit further including a comparison circuit in electrical communication with the memory and having as inputs the at least first and second values, the comparison circuit configured to provide a comparison circuit output based at least in part on the at least first and/or second values, the comparison circuit output indicative of whether the aggregate is present in the at least one channel.

12. The detection system of claim 11, wherein the first value is indicative of the one or more electrical properties of the channel circuit without the presence of a fluid in the at least one channel and the second value is indicative of the one or more electrical properties of the channel circuit with the presence of a fluid in the at least one channel.

13. The detection system of claim 11, wherein the first value is indicative of the one or more electrical properties of the channel circuit when a first potential difference is applied between the first and second electrodes in a first direction along the length of the at least one channel, and wherein the second value is indicative of the one or more electrical properties of the channel circuit when a second potential difference is applied between the first and second electrodes in a second direction along the length of the at least one channel, the second direction being opposite to the first direction.

14. The detection system of claim 11, wherein the analyte detection circuit includes one or more of: an ammeter, a voltmeter, an ohmmeter, a processor, and an equilibrium detection circuit.

15. The detection system of claim 11, wherein the one or more electrical properties includes an electrical current conducted along the length of the at least one channel between the first and second electrodes or an electrical conductance along the length of the at least one channel between the first and second electrodes.

16. The detection system of claim 11, wherein the at least one channel comprises:

a first channel comprising a first channel port and a second channel port, wherein the first channel port is in fluid communication with a first end section of the

first channel and the second channel port is in fluid communication with a second end section of the first channel; and

a second channel comprising a third channel port, wherein the first channel port is in fluid communication with a first end section of the second channel, and wherein the third channel port is in fluid communication with a second end section of the second channel.

17. The detection system of claim 11, further comprising: a voltage source for applying a potential difference using the first and second electrodes.

18. The detection system of claim 11, wherein the at least one channel is configured to have a dimension selected from a length ranging from 10 nanometers to 10 centimeters, a width ranging from 1 nanometer to 50 microns, or a depth ranging from 1 nanometer to 1 micron.

19. The detection system of claim 11, wherein the comparison circuit output is further indicative of a concentration of the analyte in the at least one channel.

20. The detection system of any one of claims 11-19, wherein the analyte is selected from the group consisting of:

a nucleic acid, and the sensor compound is a nucleic acid probe;

a silver ion, wherein the sensor compound is TPEA2; and

a mercury ion, wherein the sensor compound is TPET2.

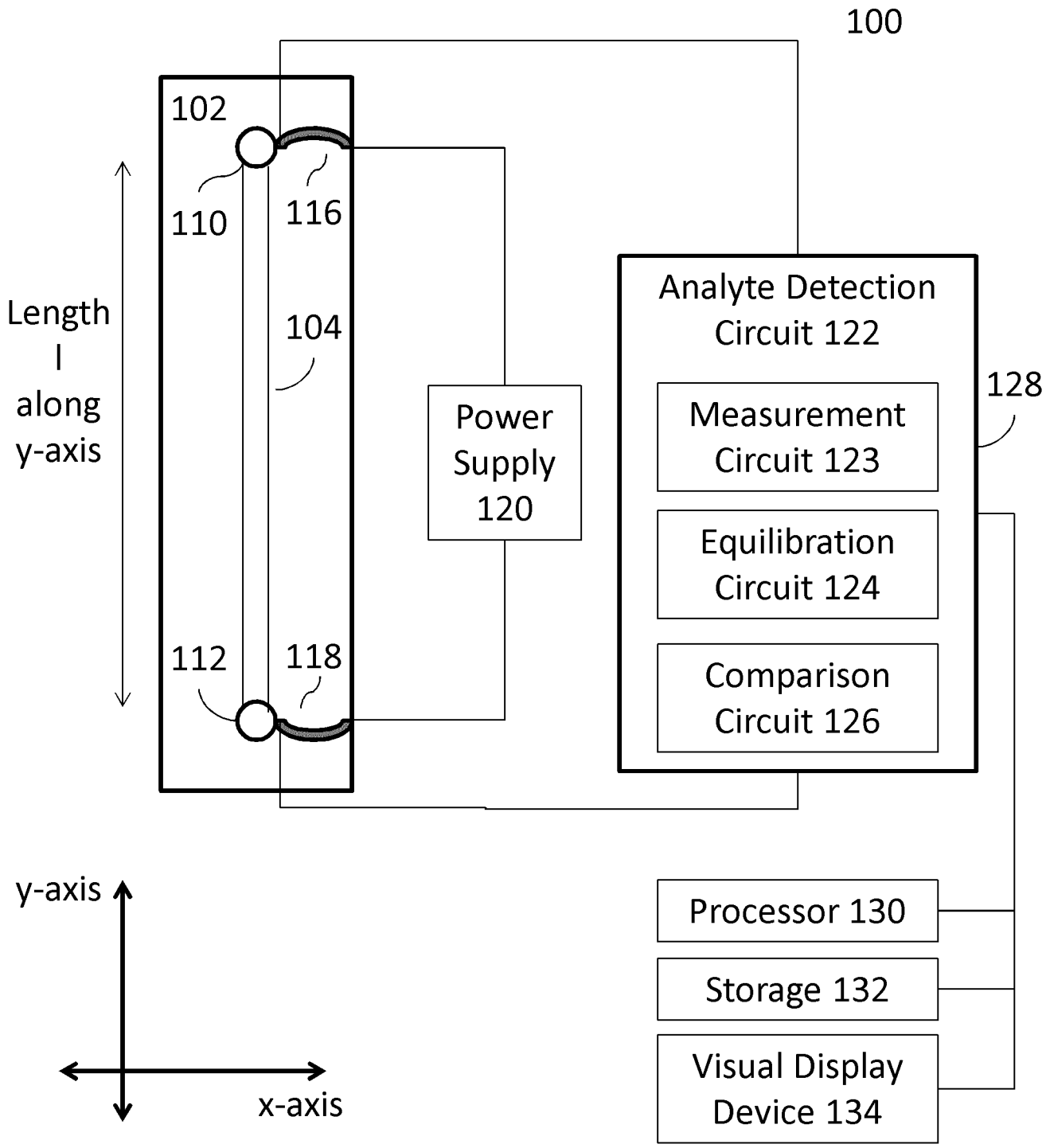

100
102
110
116
104
112
118
Length
l
along
y-axis
Power
Supply
120
Analyte Detection
Circuit 122
128
Measurement
Circuit 123
Equilibration
Circuit 124
Comparison
Circuit 126
Processor 130
Storage 132
Visual Display
Device 134
y-axis
x-axis

FIG. 1A

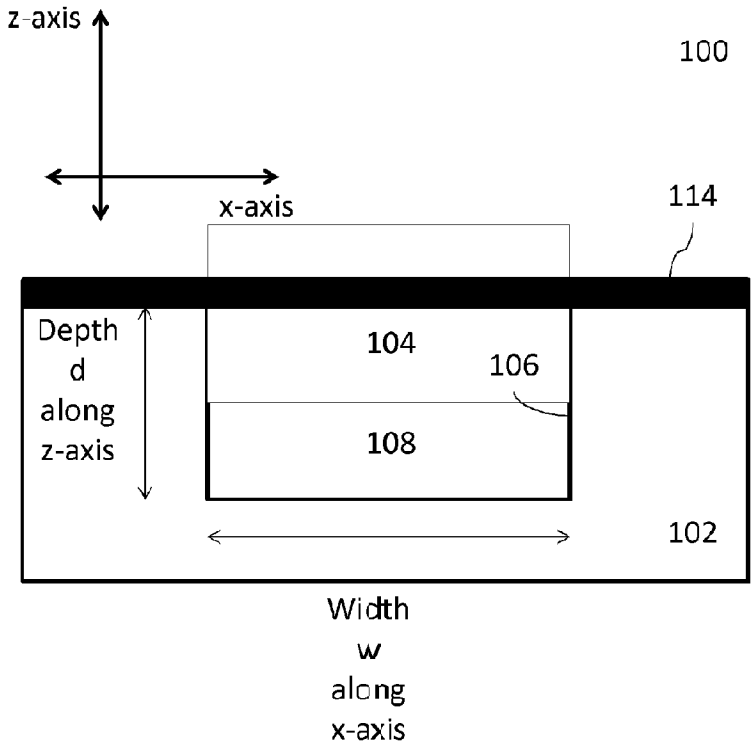

z-axis
x-axis
100
114
Depth
d
along
z-axis
104
106
108
102
Width
w
along
x-axis

FIG. 1B

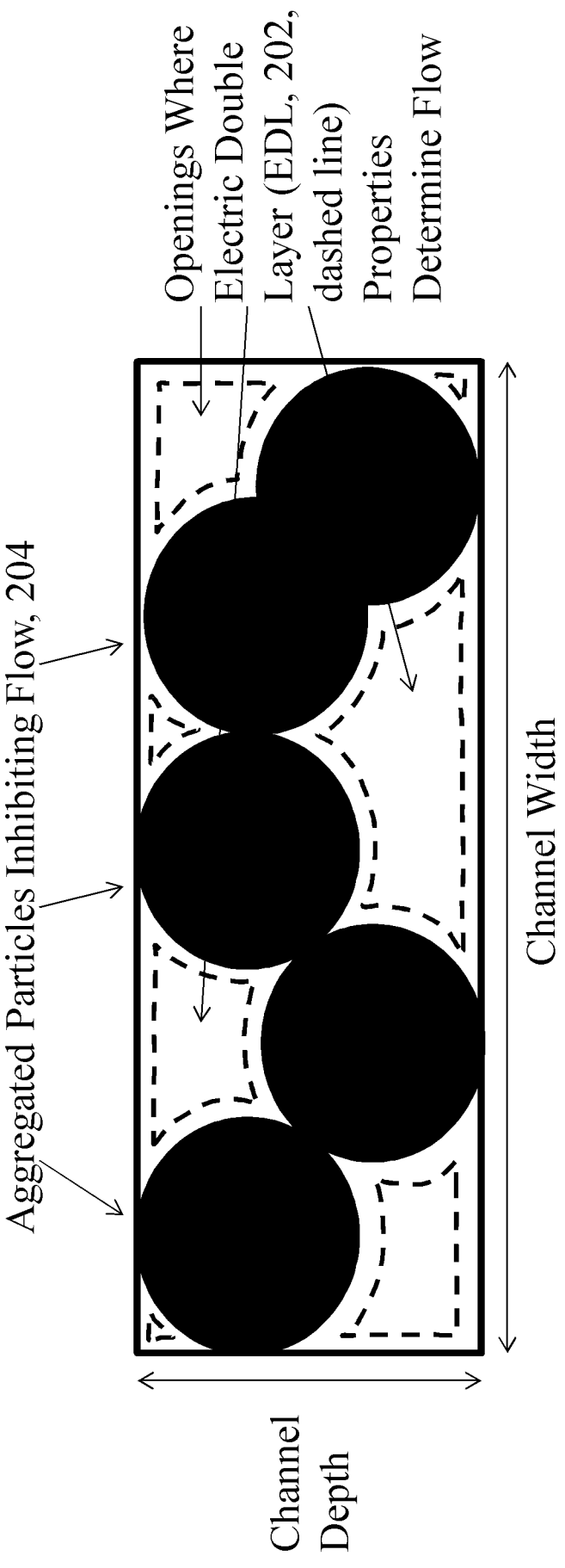

Openings Where Electric Double Layer (EDL, 202, dashed line) Properties Determine Flow
Aggregated Particles Inhibiting Flow, 204
Channel Width
Channel Depth

FIG. 2

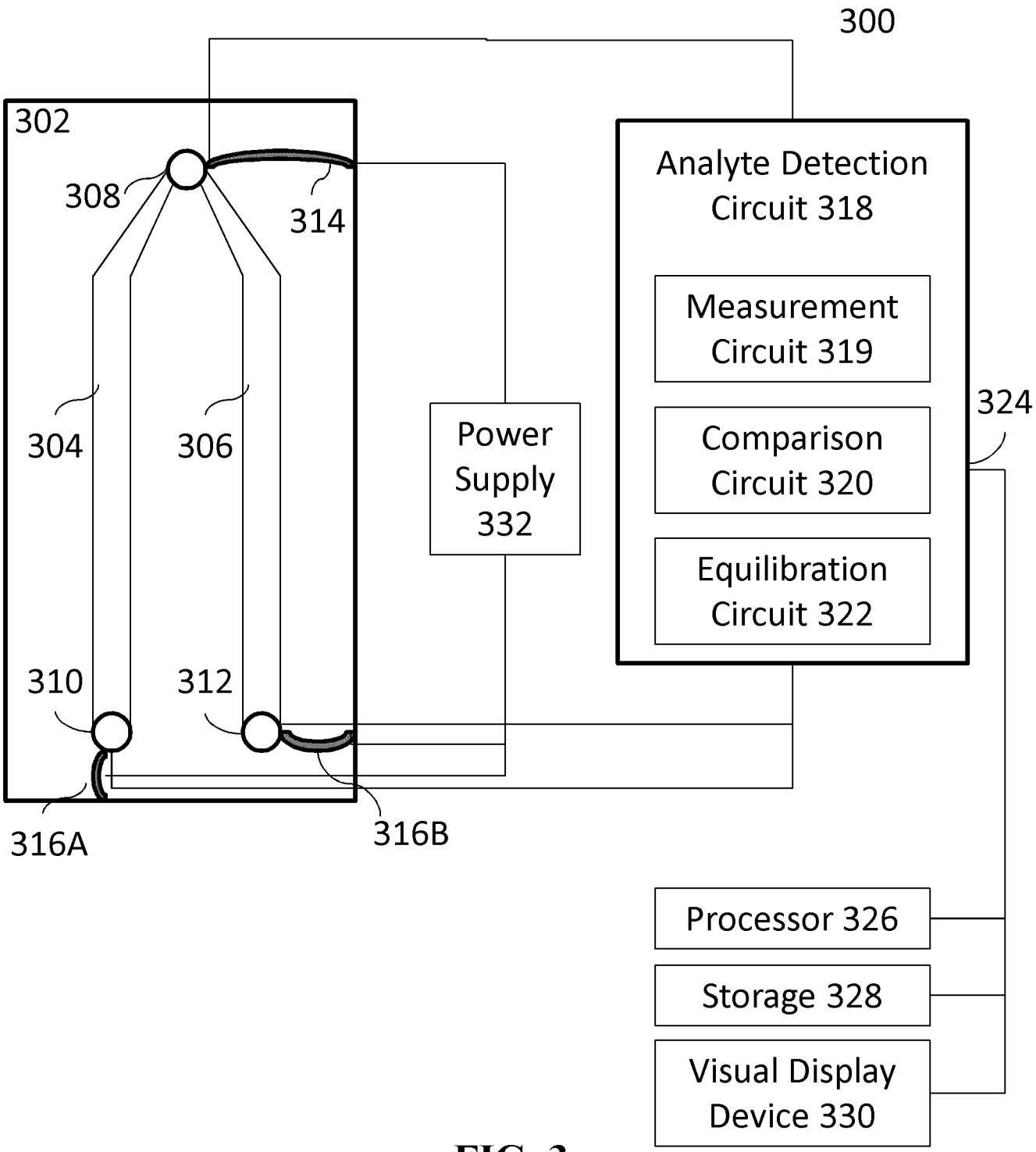

300
302
308
314
304
306
310
312
316A
316B
Power Supply 332
Analyte Detection Circuit 318
Measurement Circuit 319
Comparison Circuit 320
Equilibration Circuit 322
324
Processor 326
Storage 328
Visual Display Device 330

FIG. 3

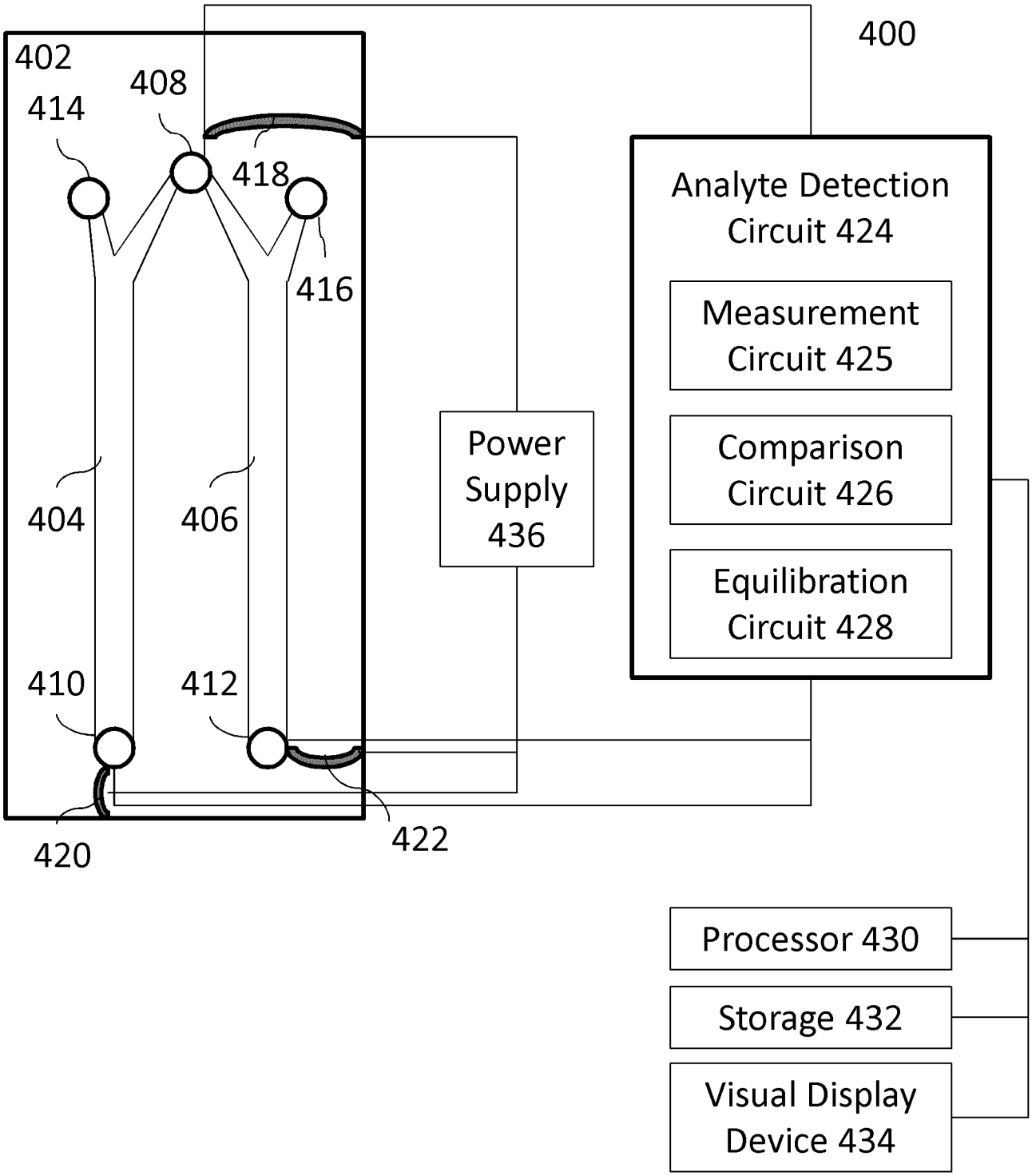

400
402
408
414
418
416
404
406
410
412
420
422
Power Supply 436
Analyte Detection Circuit 424
Measurement Circuit 425
Comparison Circuit 426
Equilibration Circuit 428
Processor 430
Storage 432
Visual Display Device 434

FIG. 4

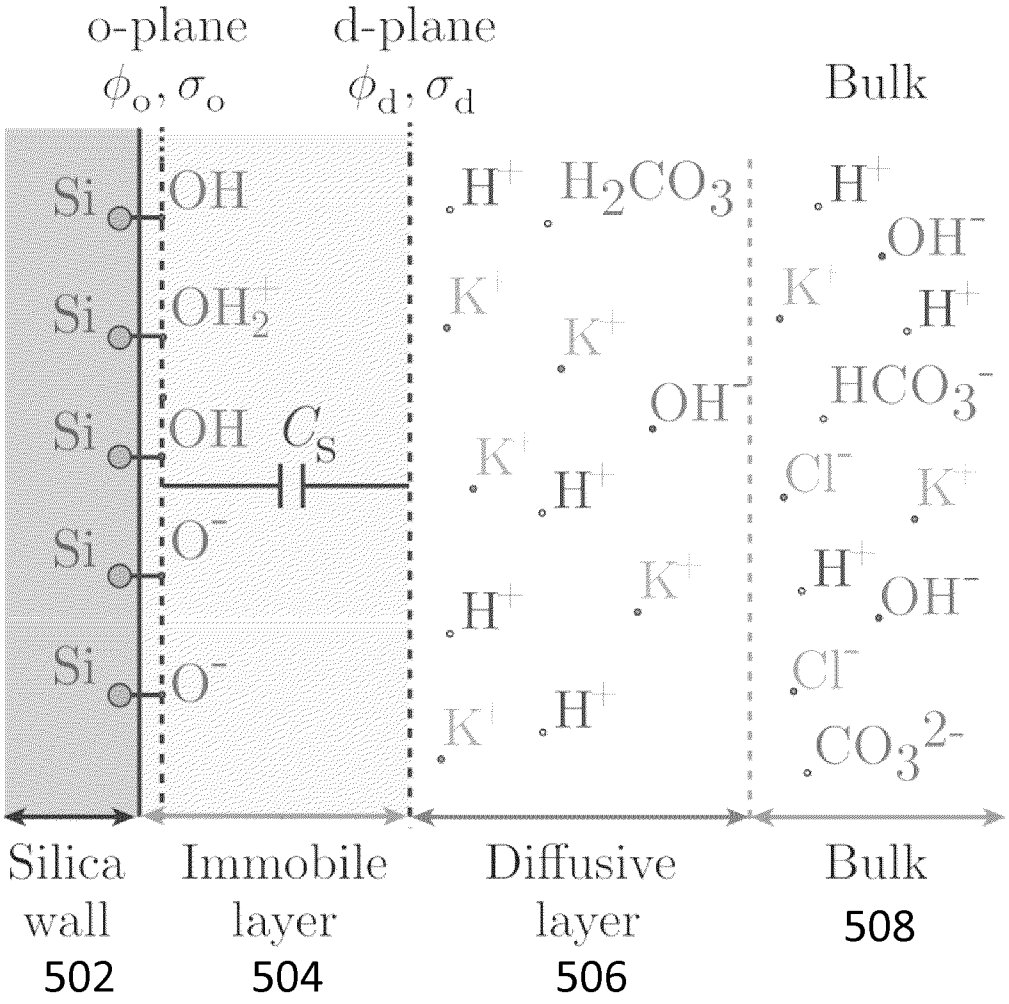

o-plane
ϕ_o, σ_o
d-plane
ϕ_d, σ_d
Bulk
Si
OH
OH_2^+
OH
C_S
O^-
O^-
H^+
H_2CO_3
K^+
OH^-
HCO_3^-
Cl^-
CO_3^{2-}
Silica wall 502
Immobile layer 504
Diffusive layer 506
Bulk 508

FIG. 5

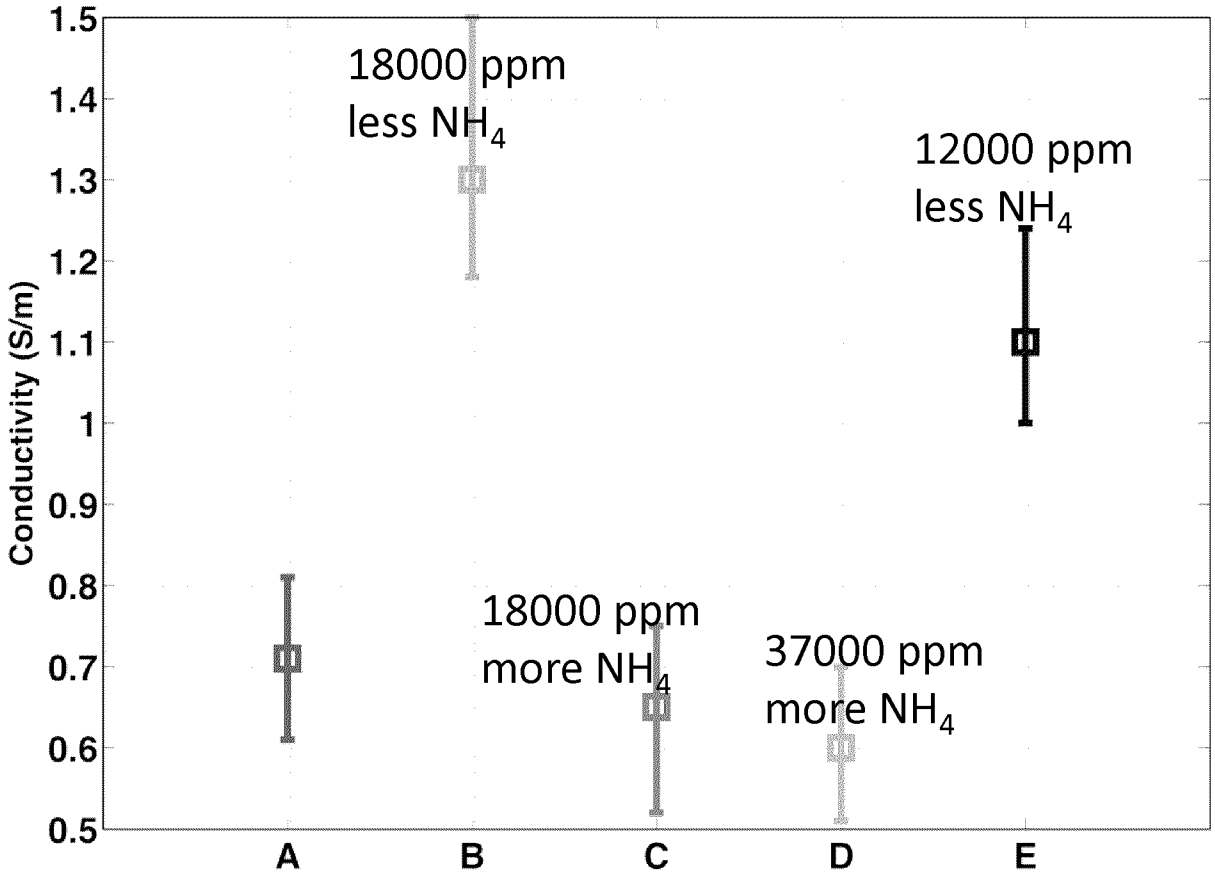

Conductivity (S/m)
1.5
1.4
1.3
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
18000 ppm less NH4
12000 ppm less NH4
18000 ppm more NH4
37000 ppm more NH4
A
B
C
D
E

FIG. 6A

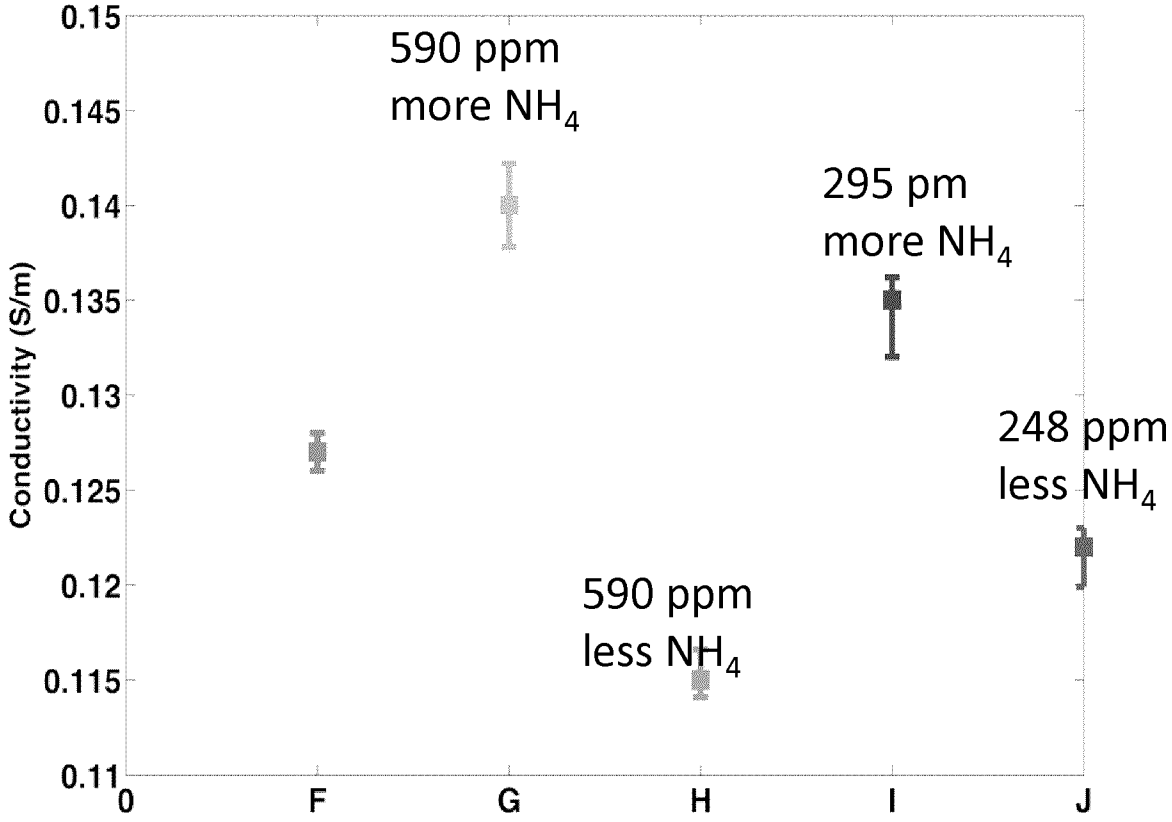

0.15
0.145
0.14
0.135
0.13
0.125
0.12
0.115
0.11
Conductivity (S/m)
0
F
G
H
I
J
590 ppm
more NH4
295 pm
more NH4
248 ppm
less NH4
590 ppm
less NH4

FIG. 6B

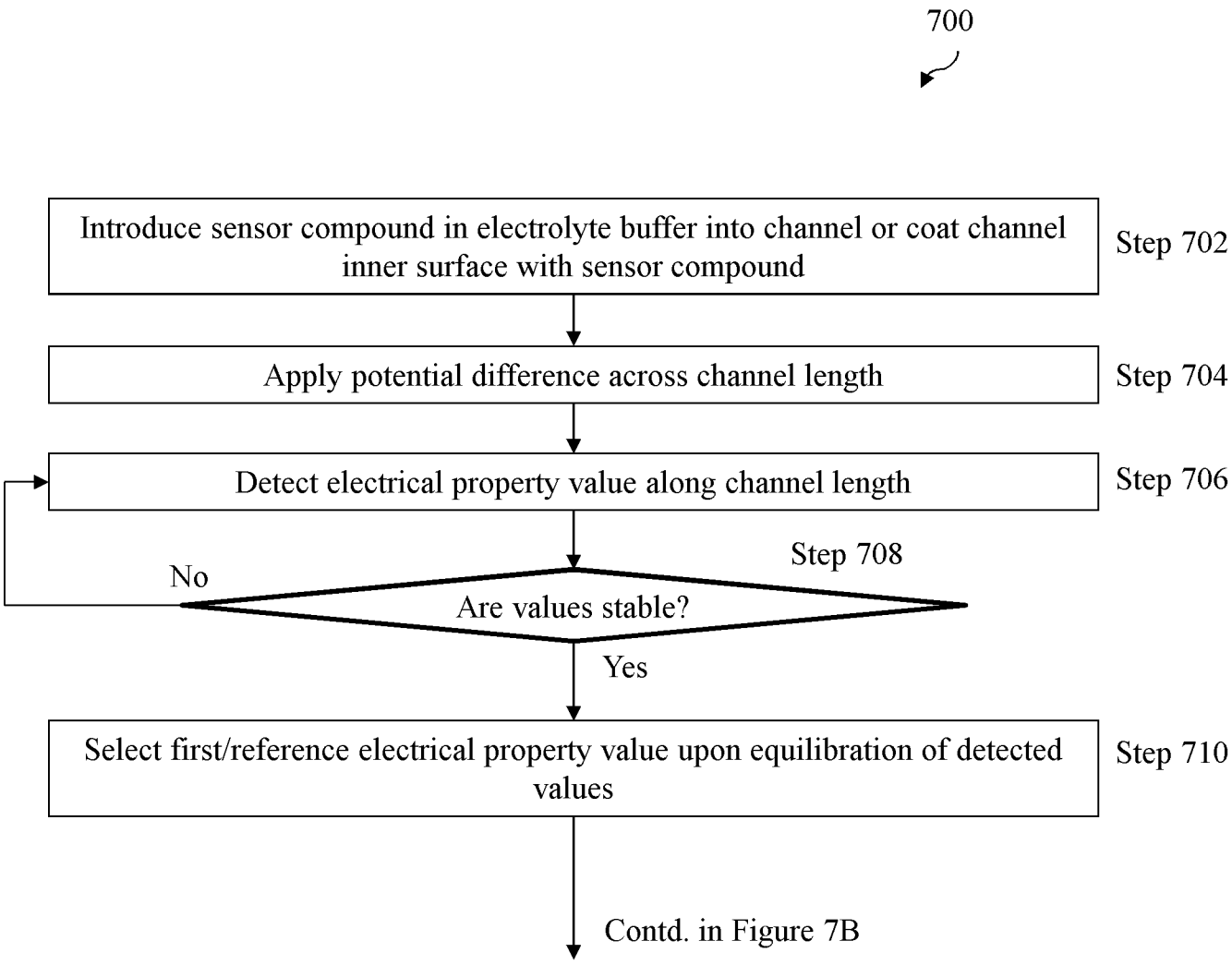

700
Introduce sensor compound in electrolyte buffer into channel or coat channel inner surface with sensor compound
Step 702
Apply potential difference across channel length
Step 704
Detect electrical property value along channel length
Step 706
Step 708
No
Are values stable?
Yes
Select first/reference electrical property value upon equilibration of detected values
Step 710
Contd. in Figure 7B

FIG. 7A

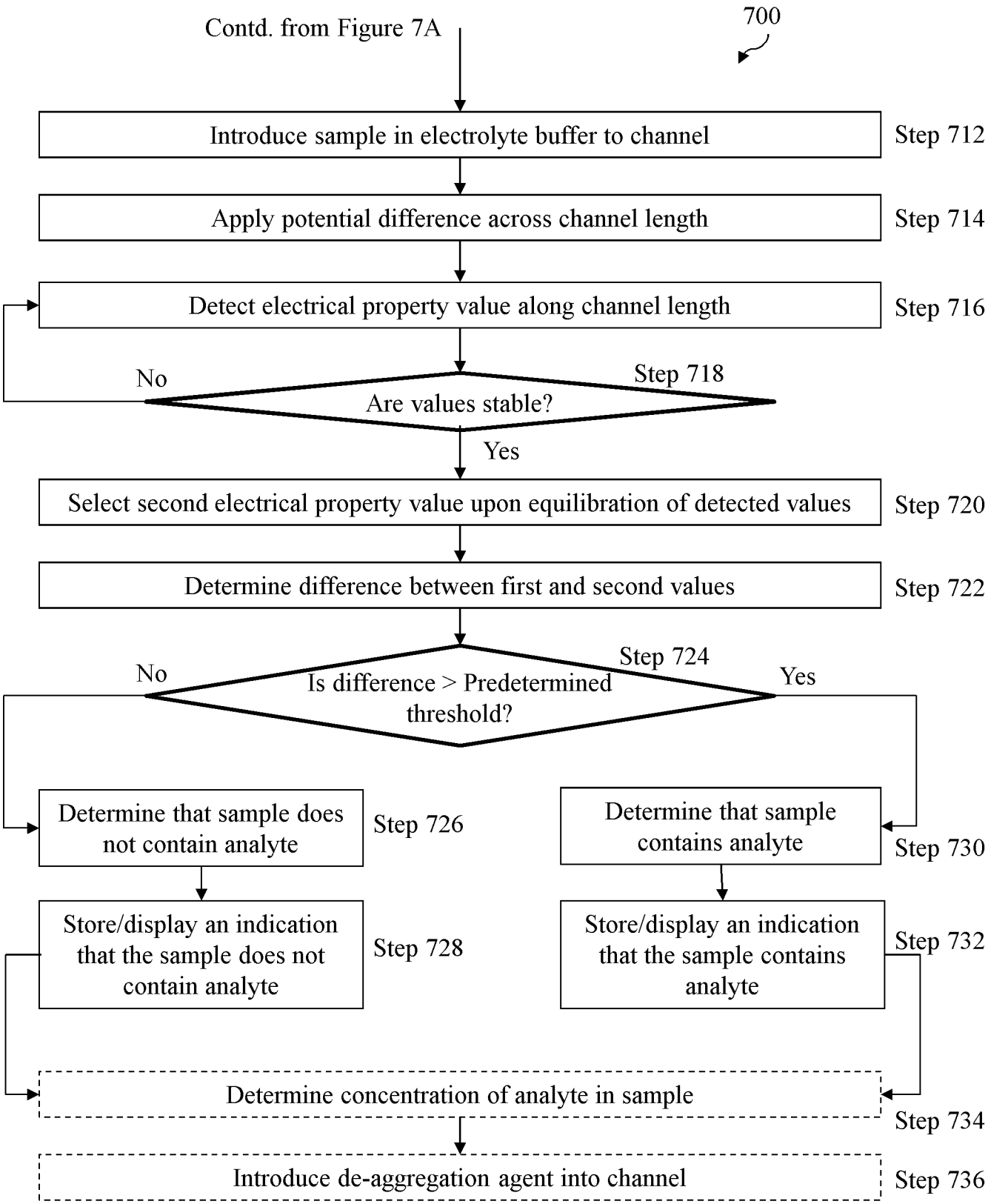

Contd. from Figure 7A
700
Introduce sample in electrolyte buffer to channel
Step 712
Apply potential difference across channel length
Step 714
Detect electrical property value along channel length
Step 716
Step 718
No
Are values stable?
Yes
Select second electrical property value upon equilibration of detected values
Step 720
Determine difference between first and second values
Step 722
Step 724
No
Is difference > Predetermined threshold?
Yes
Determine that sample does not contain analyte
Step 726
Determine that sample contains analyte
Step 730
Store/display an indication that the sample does not contain analyte
Step 728
Store/display an indication that the sample contains analyte
Step 732
Determine concentration of analyte in sample
Step 734
Introduce de-aggregation agent into channel
Step 736

FIG. 7B

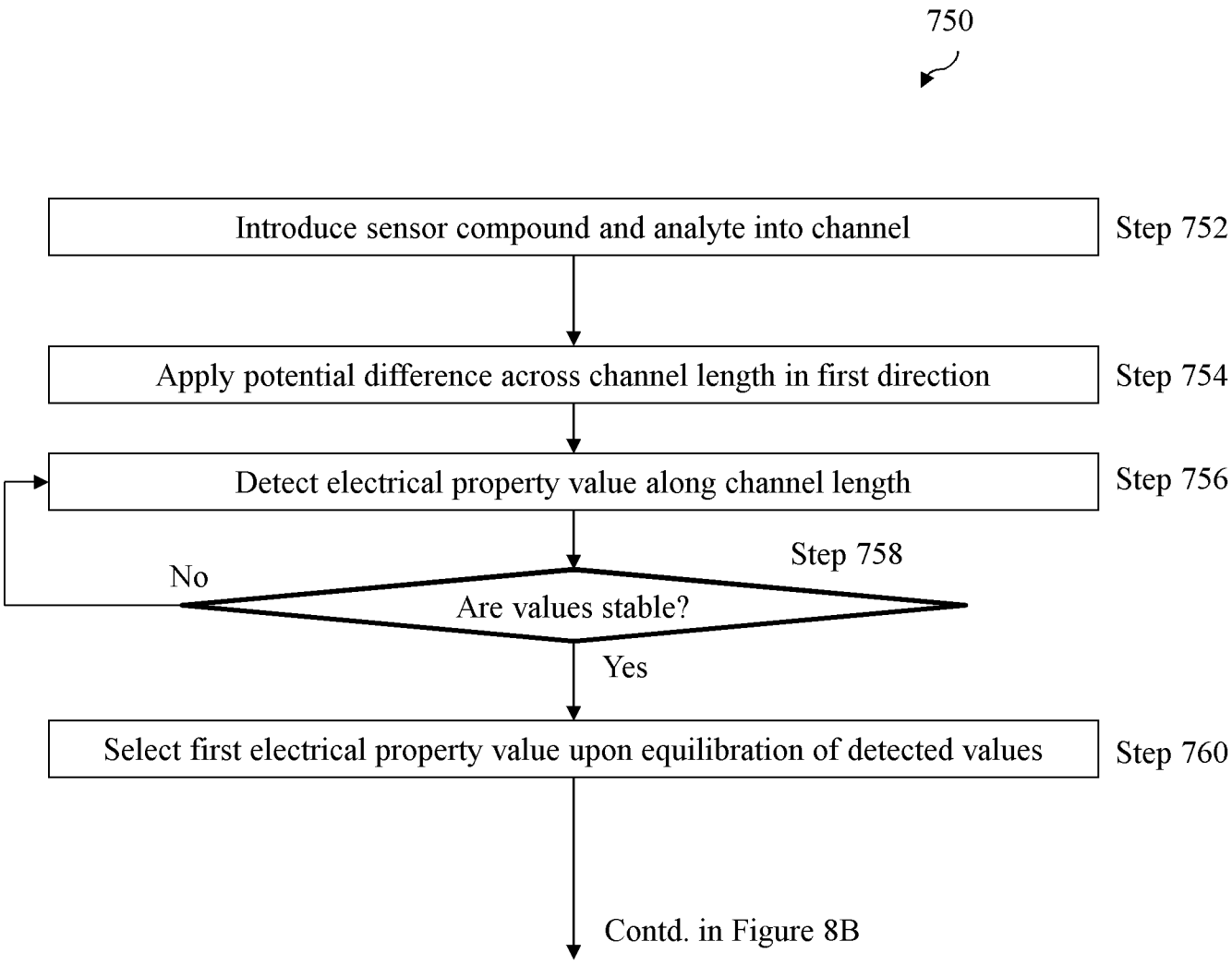

750
Introduce sensor compound and analyte into channel
Step 752
Apply potential difference across channel length in first direction
Step 754
Detect electrical property value along channel length
Step 756
Step 758
No
Are values stable?
Yes
Select first electrical property value upon equilibration of detected values
Step 760
Contd. in Figure 8B

FIG. 8A

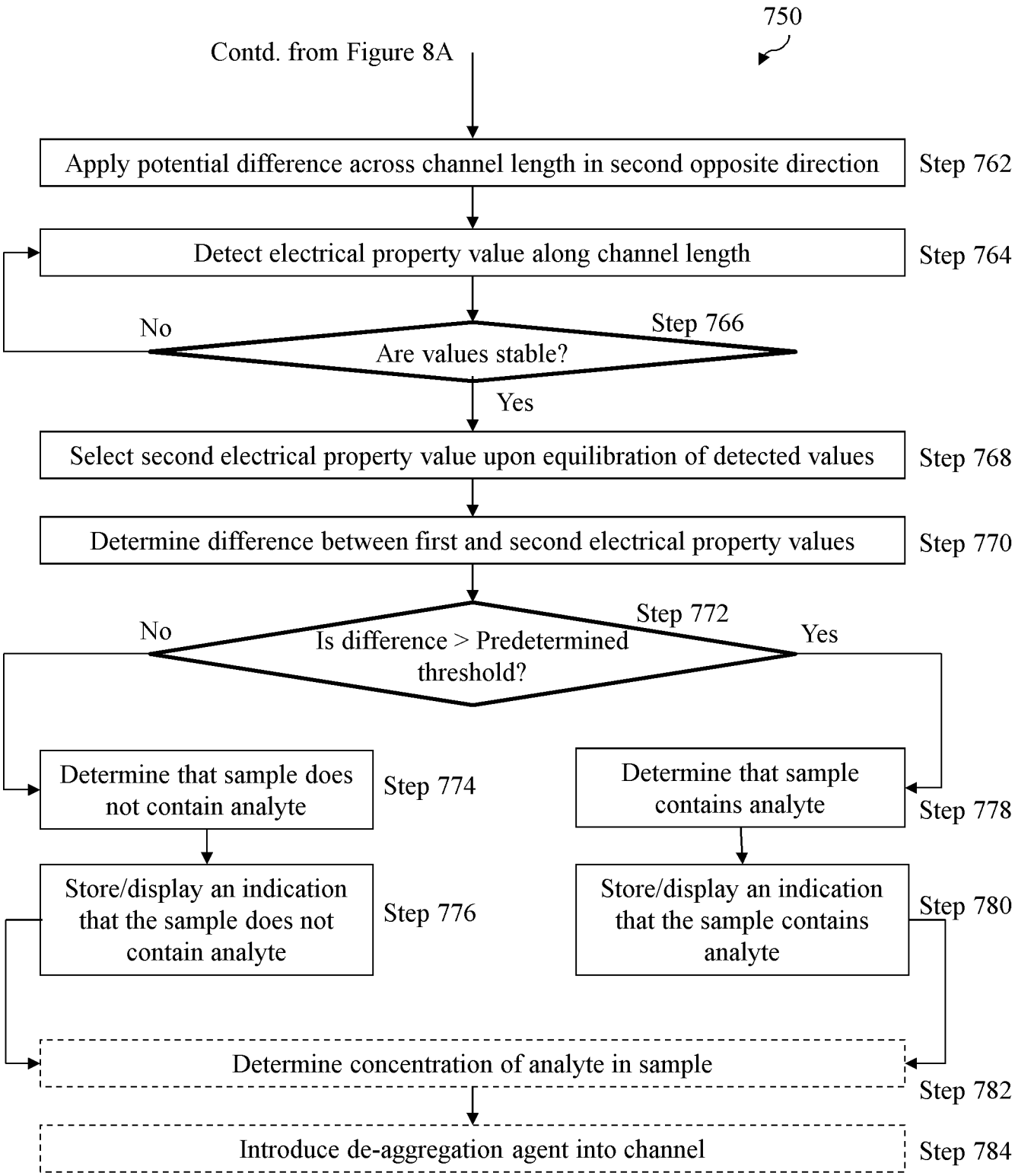

750
Contd. from Figure 8A
Apply potential difference across channel length in second opposite direction
Step 762
Detect electrical property value along channel length
Step 764
No
Step 766
Are values stable?
Yes
Select second electrical property value upon equilibration of detected values
Step 768
Determine difference between first and second electrical property values
Step 770
Step 772
No
Is difference > Predetermined threshold?
Yes
Determine that sample does not contain analyte
Step 774
Determine that sample contains analyte
Step 778
Store/display an indication that the sample does not contain analyte
Step 776
Store/display an indication that the sample contains analyte
Step 780
Determine concentration of analyte in sample
Step 782
Introduce de-aggregation agent into channel
Step 784

FIG. 8B

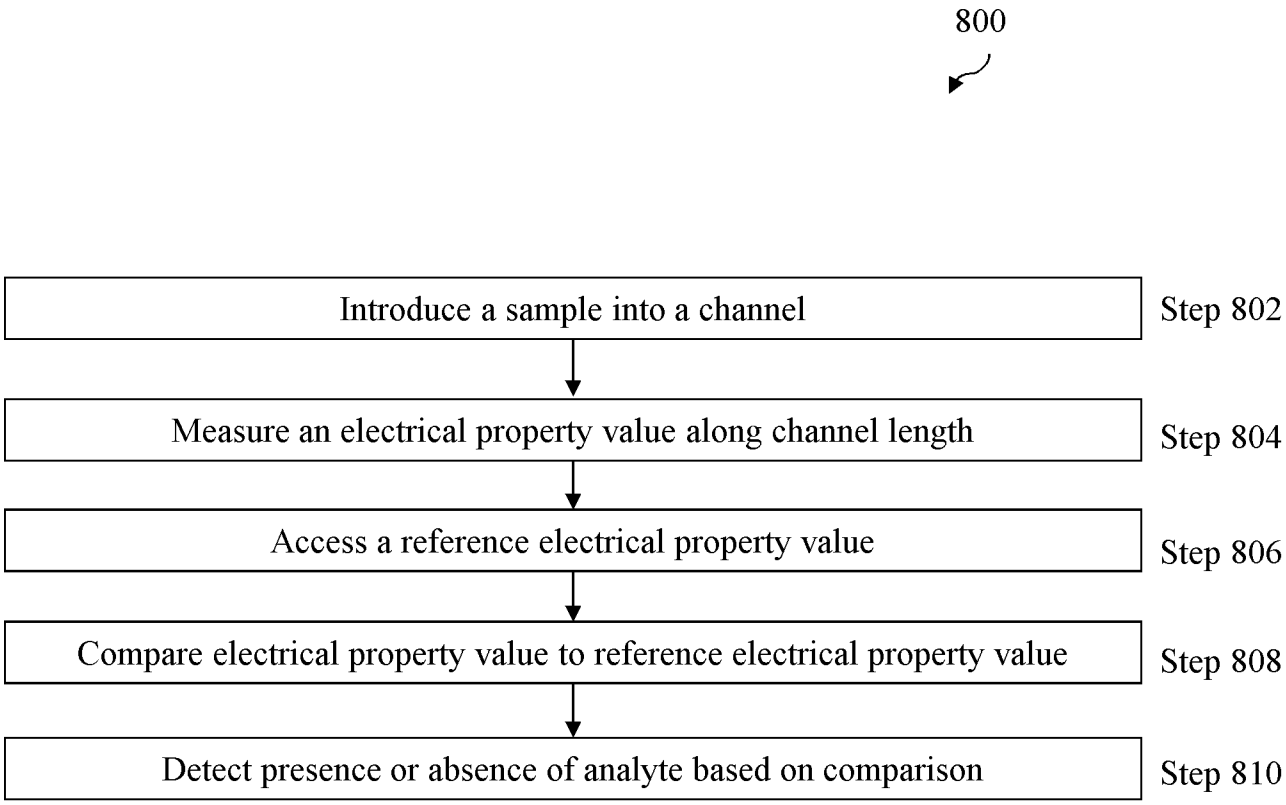

800
Introduce a sample into a channel
Step 802
Measure an electrical property value along channel length
Step 804
Access a reference electrical property value
Step 806
Compare electrical property value to reference electrical property value
Step 808
Detect presence or absence of analyte based on comparison
Step 810

FIG. 9

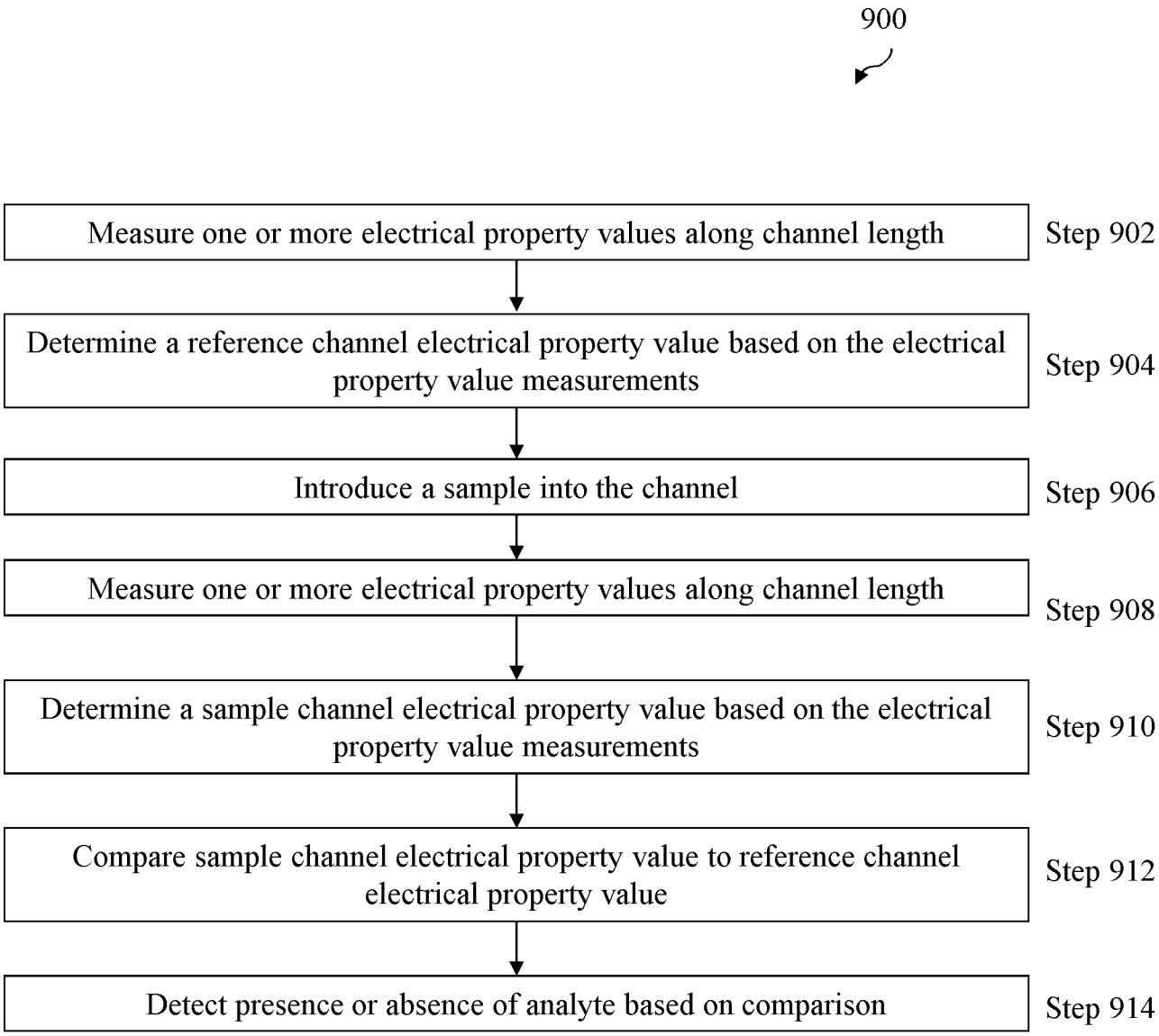

900
Measure one or more electrical property values along channel length
Step 902
Determine a reference channel electrical property value based on the electrical property value measurements
Step 904
Introduce a sample into the channel
Step 906
Measure one or more electrical property values along channel length
Step 908
Determine a sample channel electrical property value based on the electrical property value measurements
Step 910
Compare sample channel electrical property value to reference channel electrical property value
Step 912
Detect presence or absence of analyte based on comparison
Step 914

FIG. 10

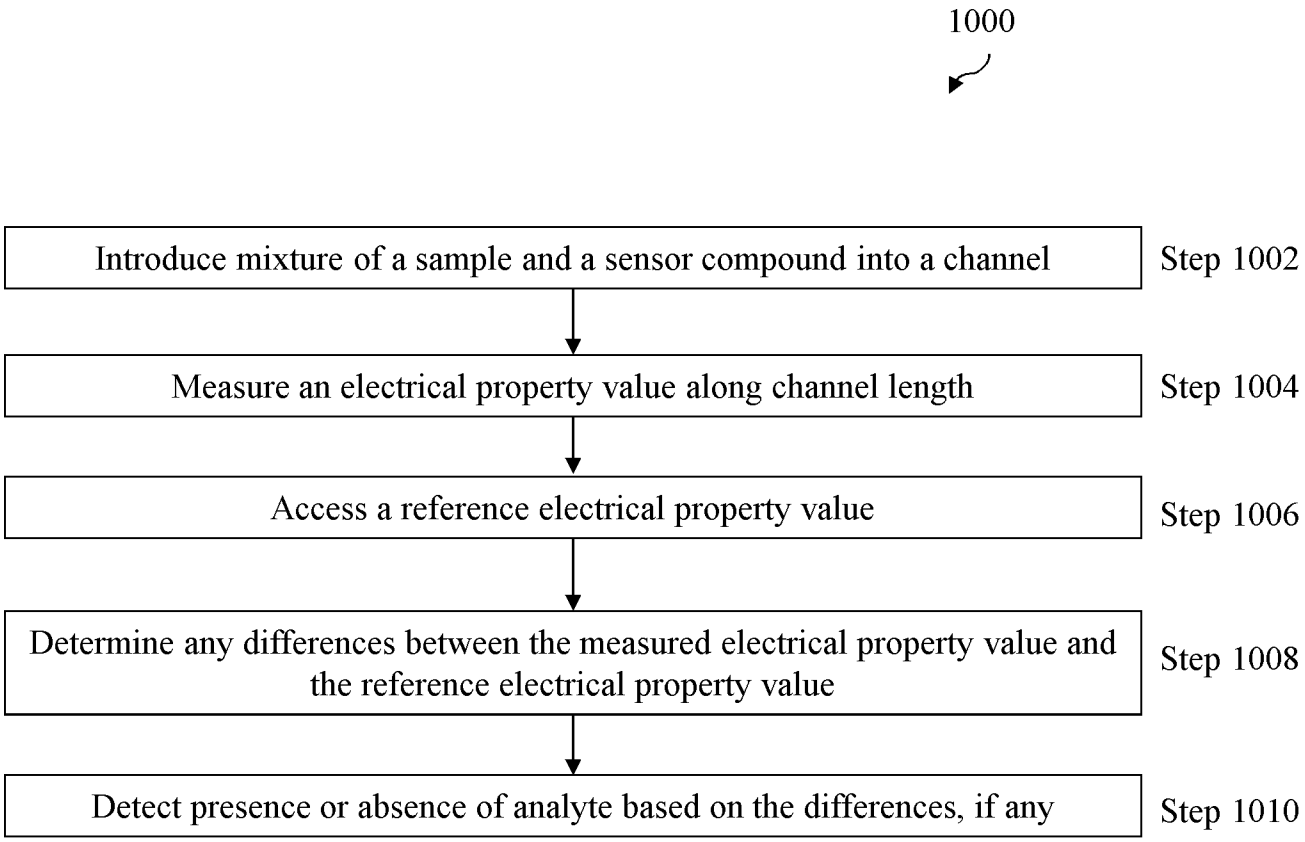

1000
Introduce mixture of a sample and a sensor compound into a channel
Step 1002
Measure an electrical property value along channel length
Step 1004
Access a reference electrical property value
Step 1006
Determine any differences between the measured electrical property value and the reference electrical property value
Step 1008
Detect presence or absence of analyte based on the differences, if any
Step 1010

FIG. 11

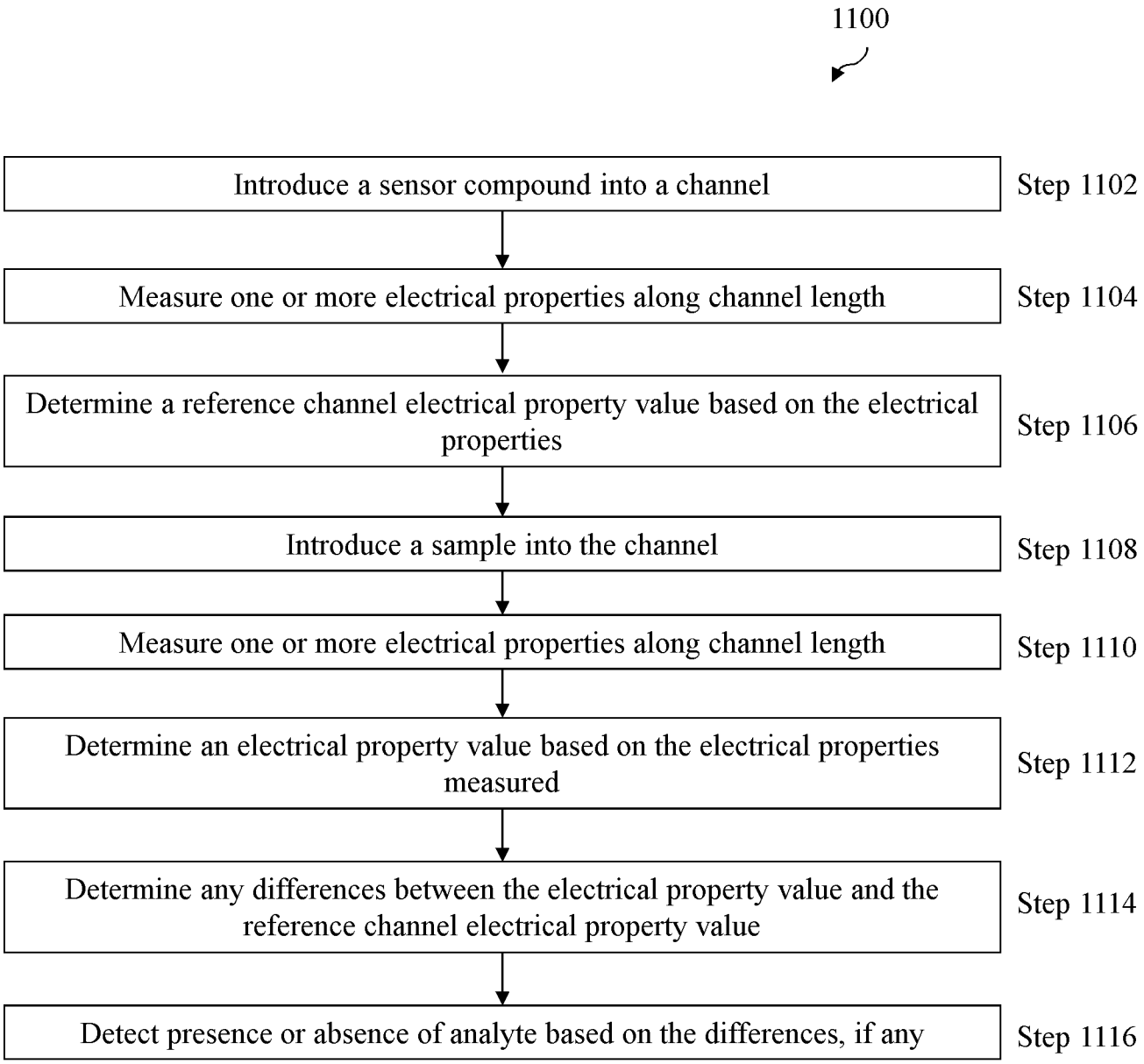

1100
Introduce a sensor compound into a channel
Step 1102
Measure one or more electrical properties along channel length
Step 1104
Determine a reference channel electrical property value based on the electrical properties
Step 1106
Introduce a sample into the channel
Step 1108
Measure one or more electrical properties along channel length
Step 1110
Determine an electrical property value based on the electrical properties measured
Step 1112
Determine any differences between the electrical property value and the reference channel electrical property value
Step 1114
Detect presence or absence of analyte based on the differences, if any
Step 1116

FIG. 12

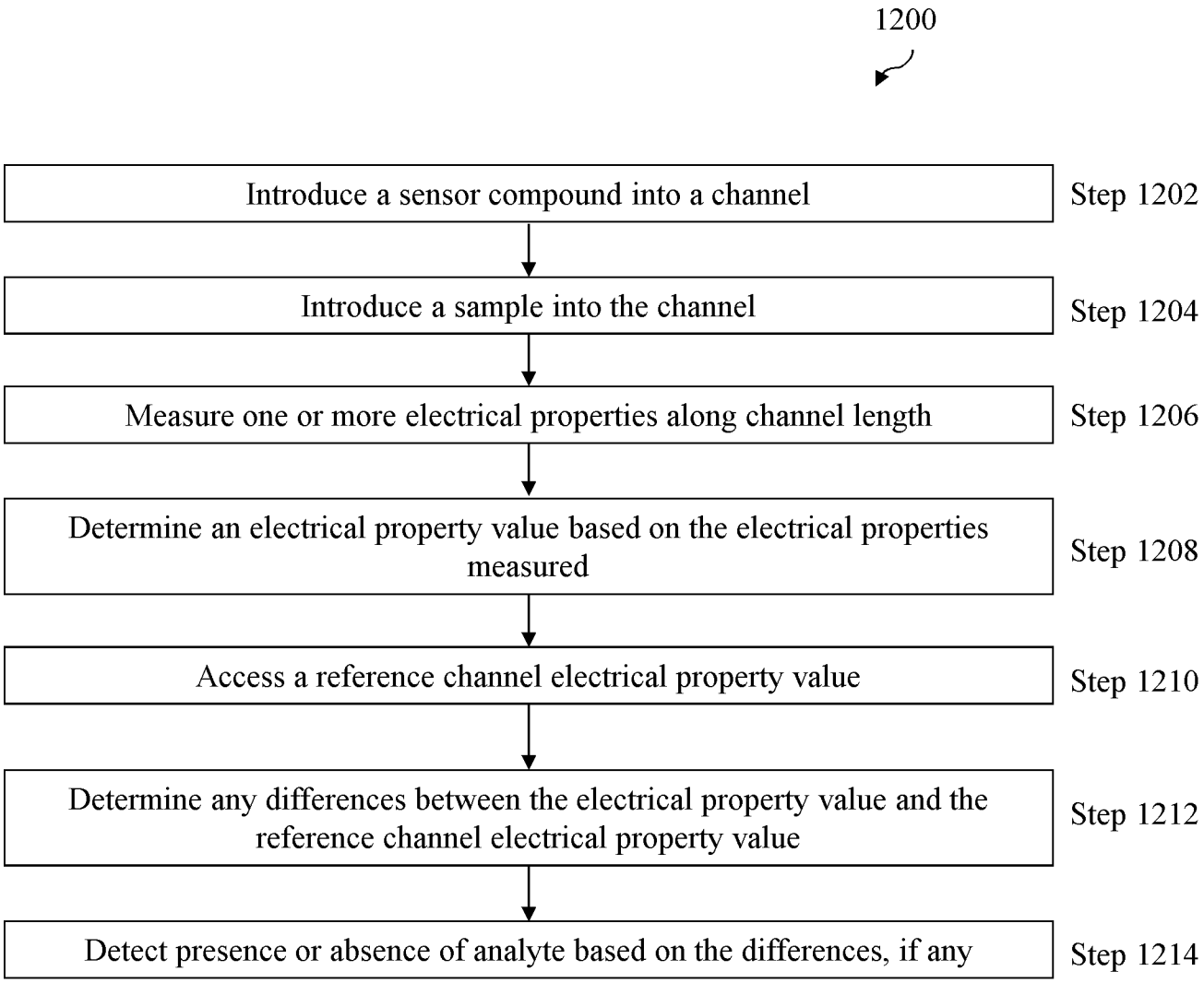

1200
Introduce a sensor compound into a channel
Step 1202
Introduce a sample into the channel
Step 1204
Measure one or more electrical properties along channel length
Step 1206
Determine an electrical property value based on the electrical properties measured
Step 1208
Access a reference channel electrical property value
Step 1210
Determine any differences between the electrical property value and the reference channel electrical property value
Step 1212
Detect presence or absence of analyte based on the differences, if any
Step 1214

FIG. 13

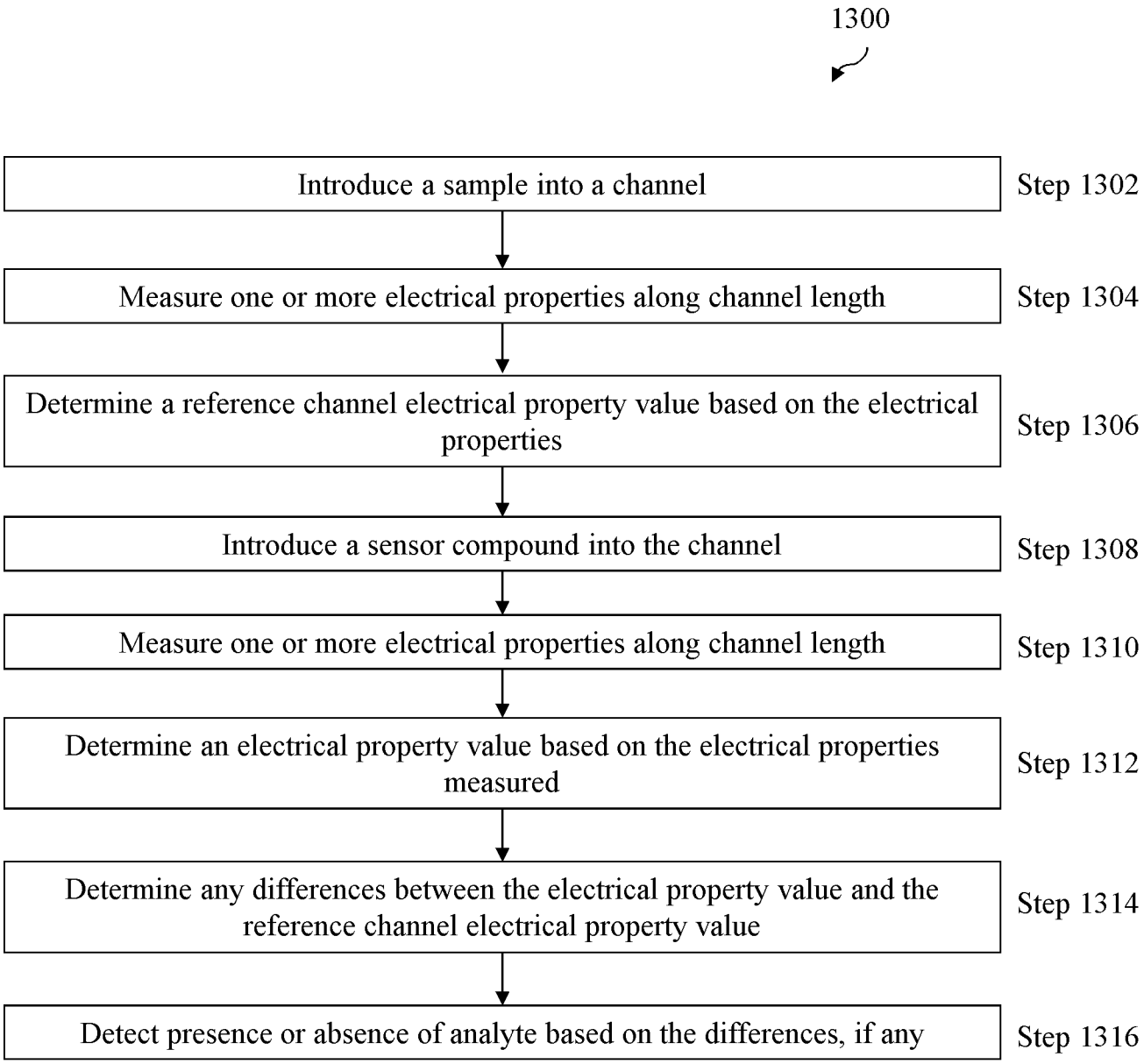

1300
Introduce a sample into a channel
Step 1302
Measure one or more electrical properties along channel length
Step 1304
Determine a reference channel electrical property value based on the electrical properties
Step 1306
Introduce a sensor compound into the channel
Step 1308
Measure one or more electrical properties along channel length
Step 1310
Determine an electrical property value based on the electrical properties measured
Step 1312
Determine any differences between the electrical property value and the reference channel electrical property value
Step 1314
Detect presence or absence of analyte based on the differences, if any
Step 1316

FIG. 14

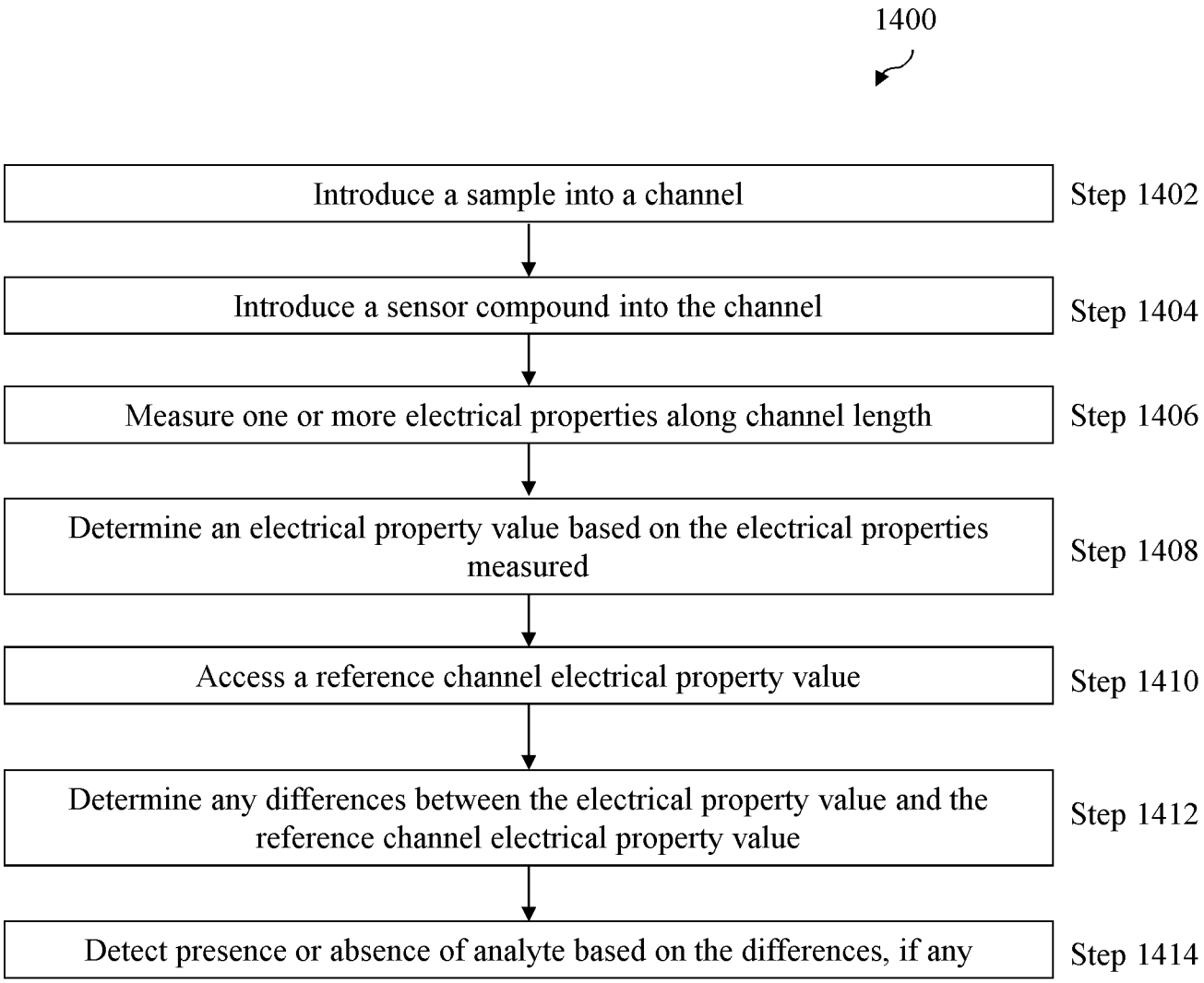

1400
Introduce a sample into a channel
Step 1402
Introduce a sensor compound into the channel
Step 1404
Measure one or more electrical properties along channel length
Step 1406
Determine an electrical property value based on the electrical properties measured
Step 1408
Access a reference channel electrical property value
Step 1410
Determine any differences between the electrical property value and the reference channel electrical property value
Step 1412
Detect presence or absence of analyte based on the differences, if any
Step 1414

FIG. 15

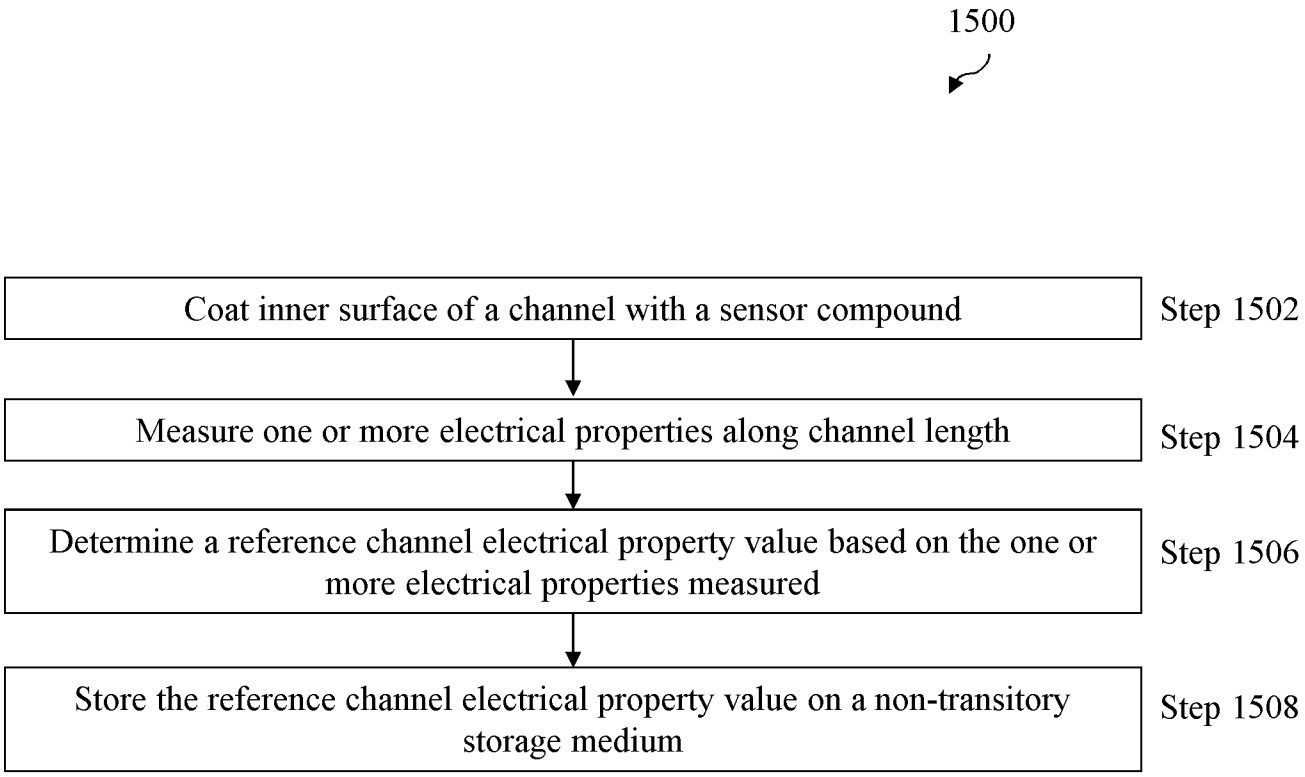

1500
Coat inner surface of a channel with a sensor compound
Step 1502
Measure one or more electrical properties along channel length
Step 1504
Determine a reference channel electrical property value based on the one or more electrical properties measured
Step 1506
Store the reference channel electrical property value on a non-transitory storage medium
Step 1508

FIG. 16

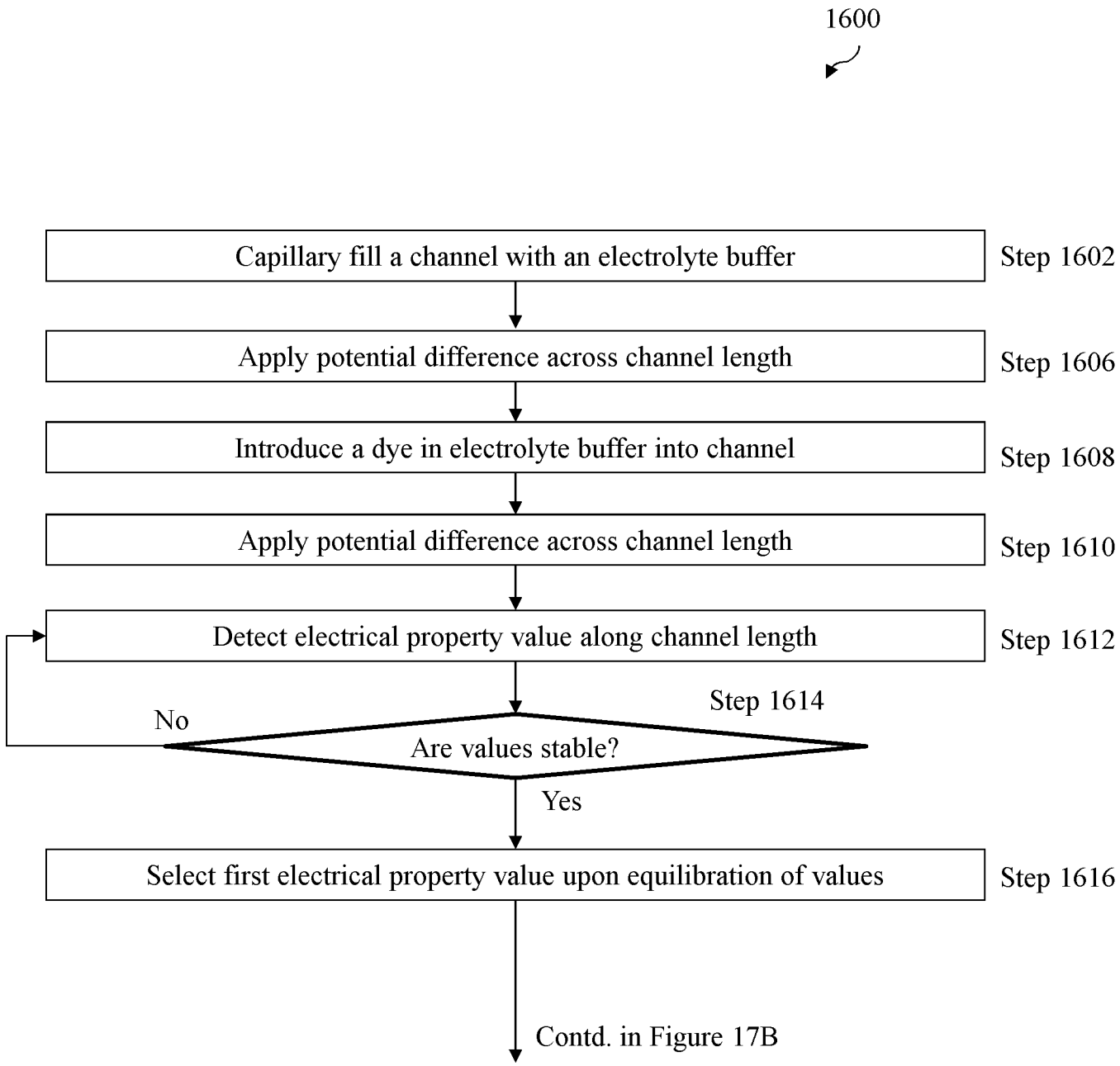

1600
Capillary fill a channel with an electrolyte buffer
Step 1602
Apply potential difference across channel length
Step 1606
Introduce a dye in electrolyte buffer into channel
Step 1608
Apply potential difference across channel length
Step 1610
Detect electrical property value along channel length
Step 1612
Step 1614
No
Are values stable?
Yes
Select first electrical property value upon equilibration of values
Step 1616
Contd. in Figure 17B

FIG. 17A

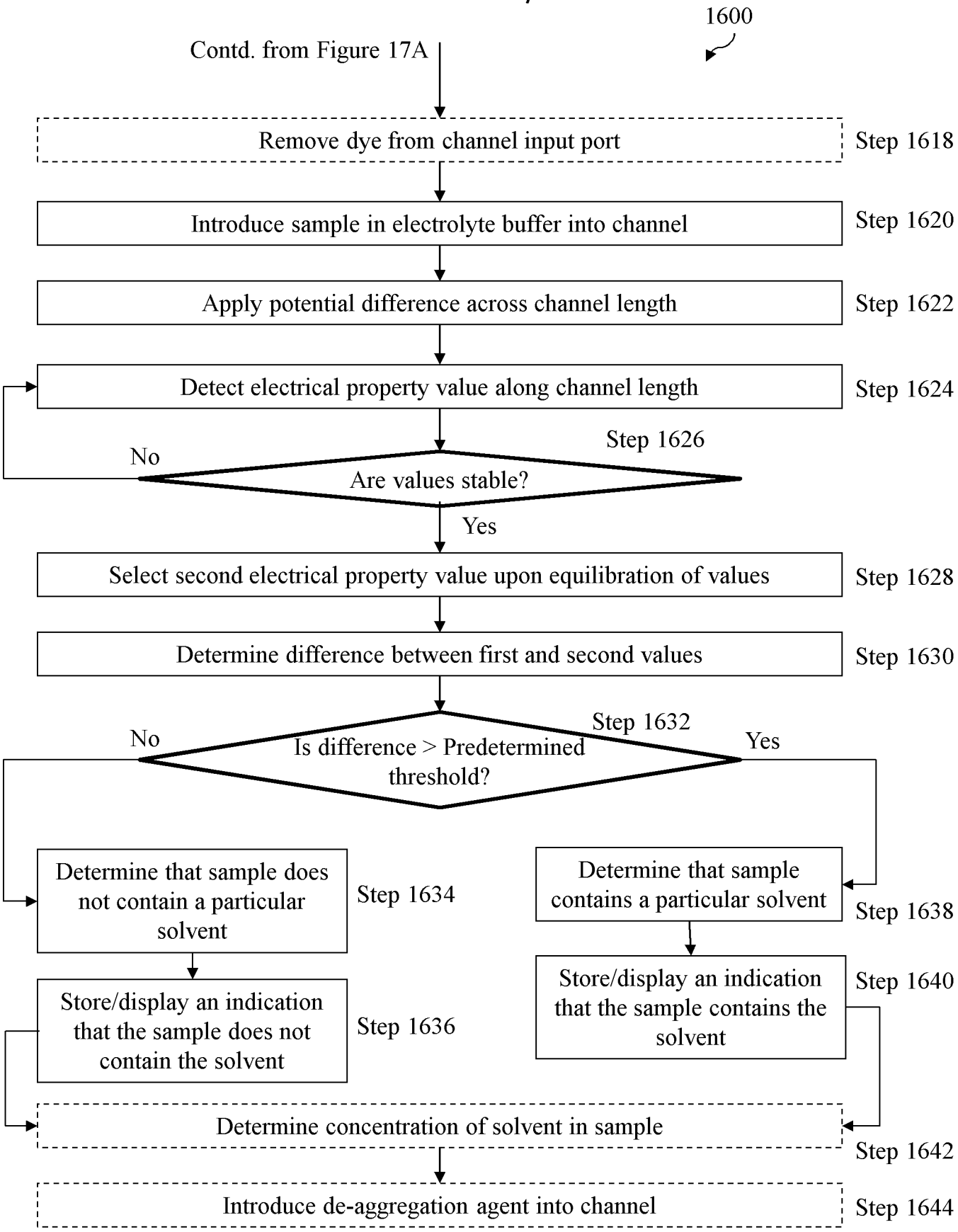

1600
Contd. from Figure 17A
Remove dye from channel input port
Step 1618
Introduce sample in electrolyte buffer into channel
Step 1620
Apply potential difference across channel length
Step 1622
Detect electrical property value along channel length
Step 1624
Step 1626
No
Are values stable?
Yes
Select second electrical property value upon equilibration of values
Step 1628
Determine difference between first and second values
Step 1630
Step 1632
No
Is difference > Predetermined threshold?
Yes
Determine that sample does not contain a particular solvent
Step 1634
Store/display an indication that the sample does not contain the solvent
Step 1636
Determine that sample contains a particular solvent
Step 1638
Store/display an indication that the sample contains the solvent
Step 1640
Determine concentration of solvent in sample
Step 1642
Introduce de-aggregation agent into channel
Step 1644

FIG. 17B

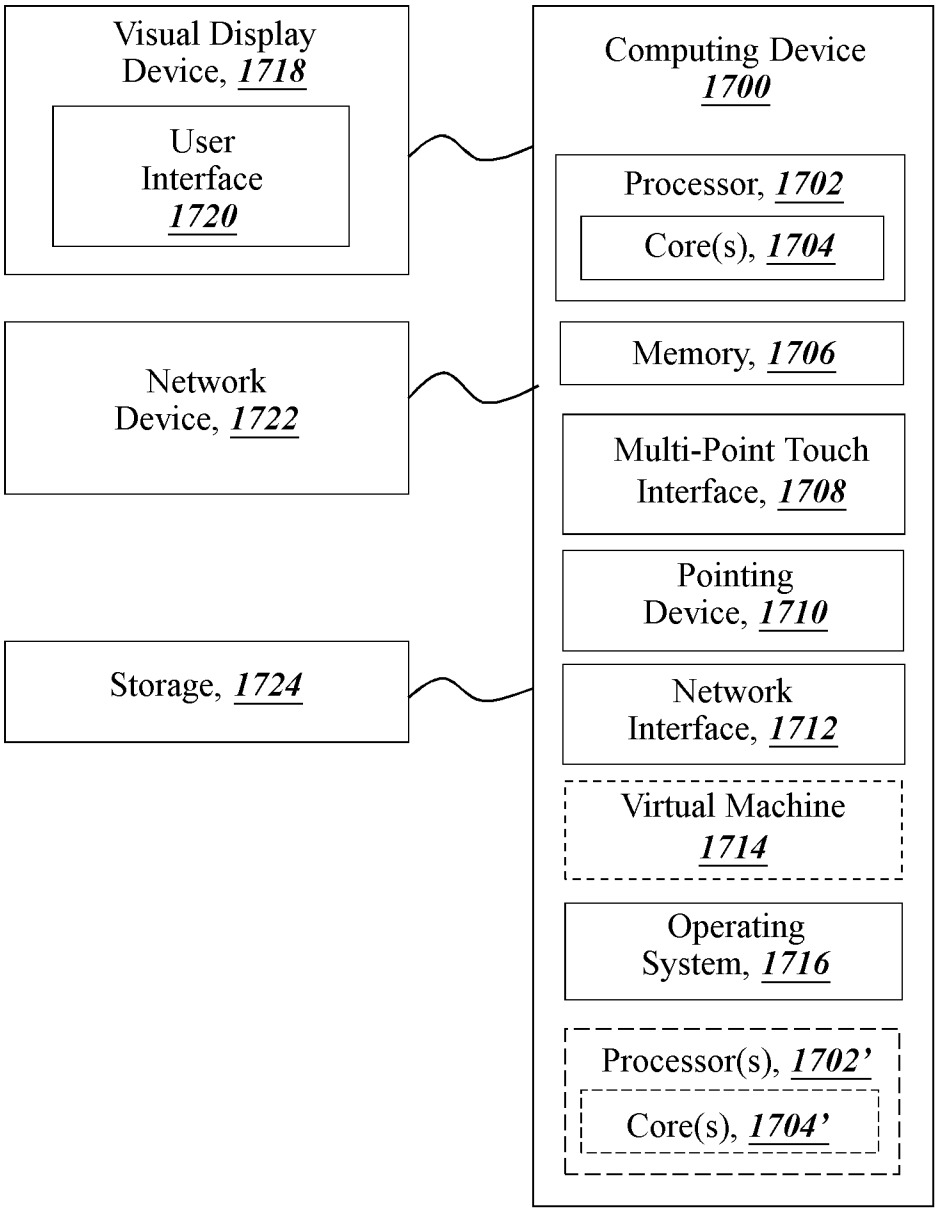

Visual Display Device, 1718
User Interface 1720
Network Device, 1722
Storage, 1724
Computing Device 1700
Processor, 1702
Core(s), 1704
Memory, 1706
Multi-Point Touch Interface, 1708
Pointing Device, 1710
Network Interface, 1712
Virtual Machine 1714
Operating System, 1716
Processor(s), 1702'
Core(s), 1704'

FIG. 18

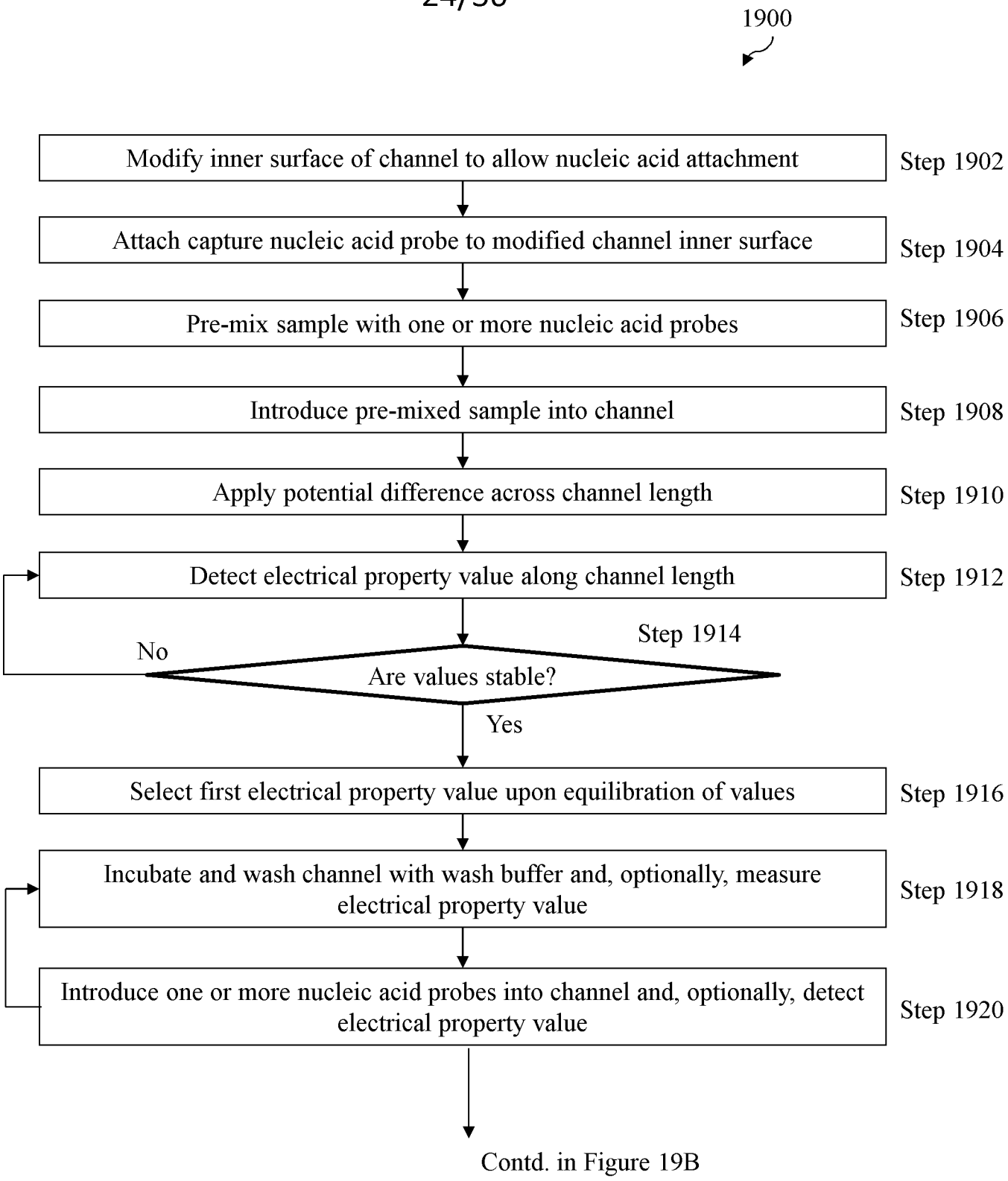

1900
Modify inner surface of channel to allow nucleic acid attachment
Step 1902
Attach capture nucleic acid probe to modified channel inner surface
Step 1904
Pre-mix sample with one or more nucleic acid probes
Step 1906
Introduce pre-mixed sample into channel
Step 1908
Apply potential difference across channel length
Step 1910
Detect electrical property value along channel length
Step 1912
Step 1914
No
Are values stable?
Yes
Select first electrical property value upon equilibration of values
Step 1916
Incubate and wash channel with wash buffer and, optionally, measure electrical property value
Step 1918
Introduce one or more nucleic acid probes into channel and, optionally, detect electrical property value
Step 1920
Contd. in Figure 19B

FIG. 19A

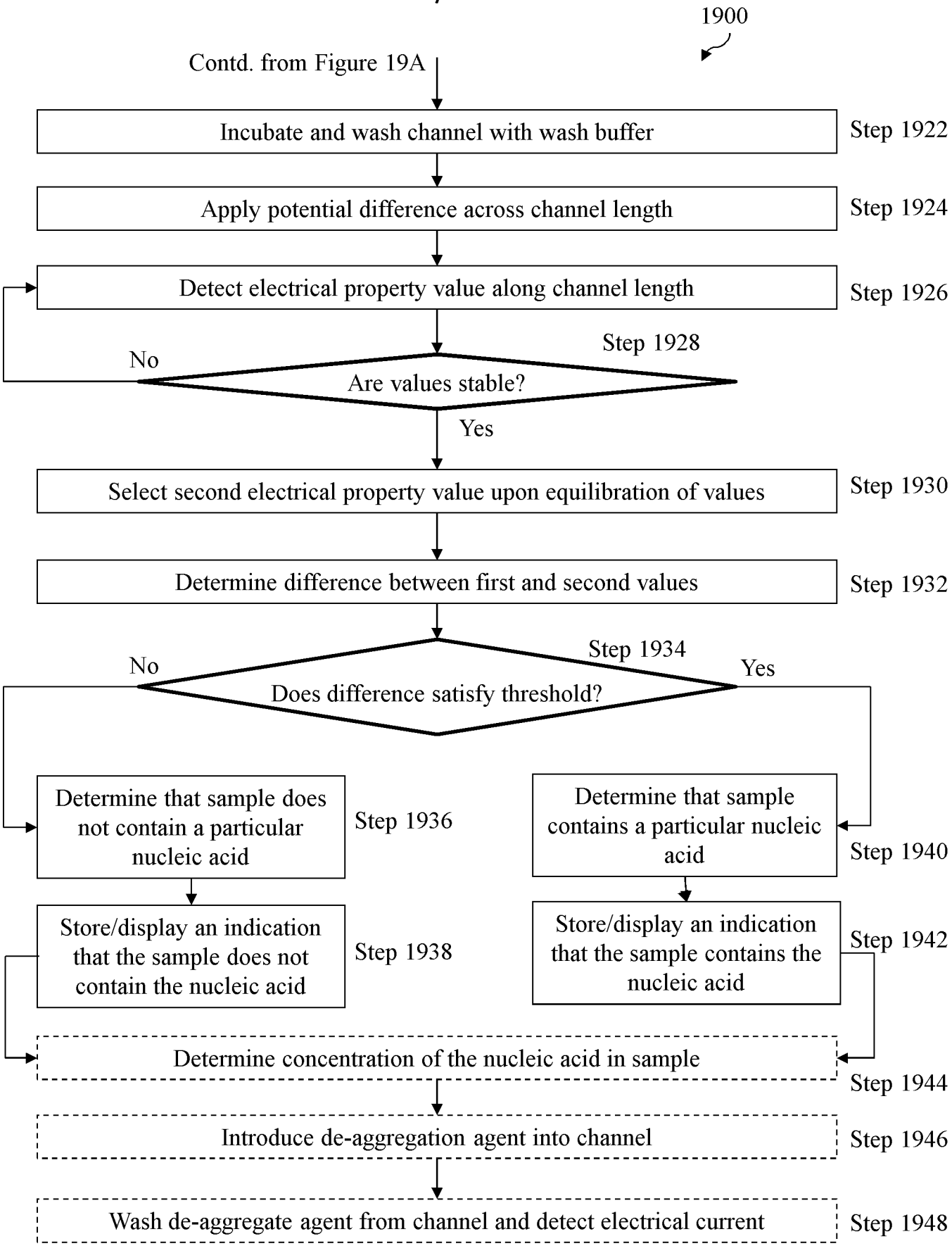

1900
Contd. from Figure 19A
Incubate and wash channel with wash buffer
Step 1922
Apply potential difference across channel length
Step 1924
Detect electrical property value along channel length
Step 1926
Step 1928
No
Are values stable?
Yes
Select second electrical property value upon equilibration of values
Step 1930
Determine difference between first and second values
Step 1932
Step 1934
No
Does difference satisfy threshold?
Yes
Determine that sample does not contain a particular nucleic acid
Step 1936
Determine that sample contains a particular nucleic acid
Step 1940
Store/display an indication that the sample does not contain the nucleic acid
Step 1938
Store/display an indication that the sample contains the nucleic acid
Step 1942
Determine concentration of the nucleic acid in sample
Step 1944
Introduce de-aggregation agent into channel
Step 1946
Wash de-aggregate agent from channel and detect electrical current
Step 1948

FIG. 19B

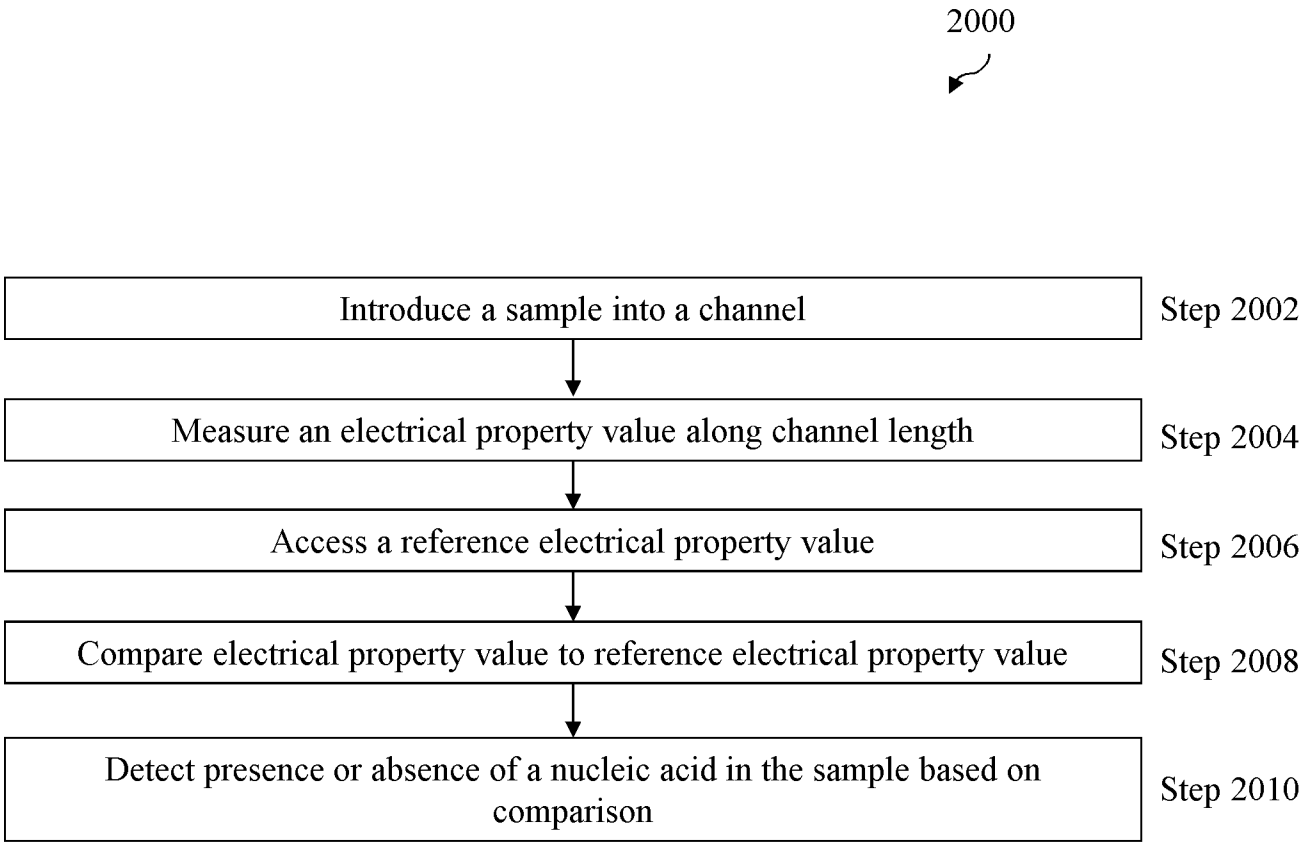

2000
Introduce a sample into a channel
Step 2002
Measure an electrical property value along channel length
Step 2004
Access a reference electrical property value
Step 2006
Compare electrical property value to reference electrical property value
Step 2008
Detect presence or absence of a nucleic acid in the sample based on comparison
Step 2010

FIG. 20

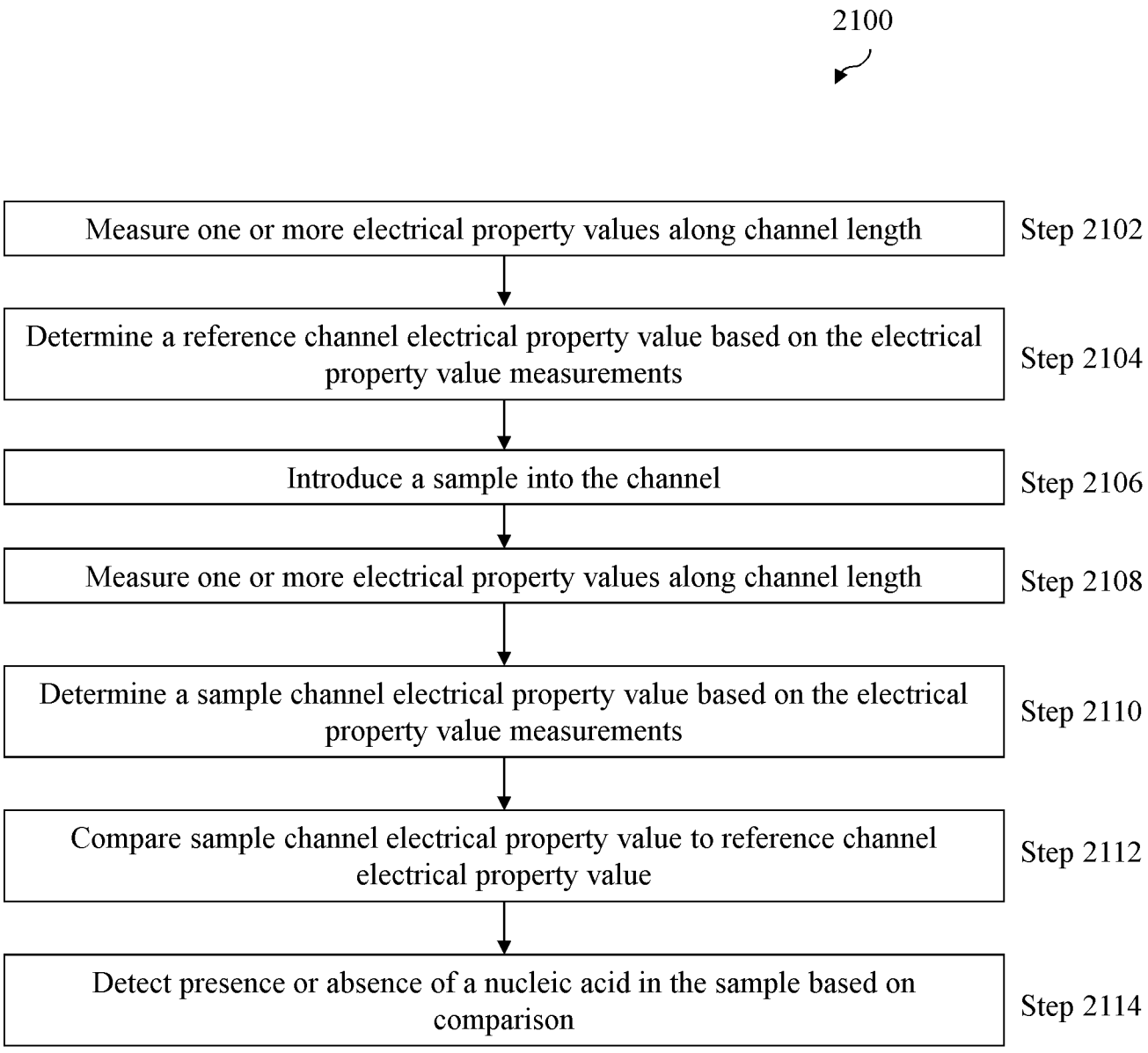

2100
Measure one or more electrical property values along channel length
Step 2102
Determine a reference channel electrical property value based on the electrical property value measurements
Step 2104
Introduce a sample into the channel
Step 2106
Measure one or more electrical property values along channel length
Step 2108
Determine a sample channel electrical property value based on the electrical property value measurements
Step 2110
Compare sample channel electrical property value to reference channel electrical property value
Step 2112
Detect presence or absence of a nucleic acid in the sample based on comparison
Step 2114

FIG. 21

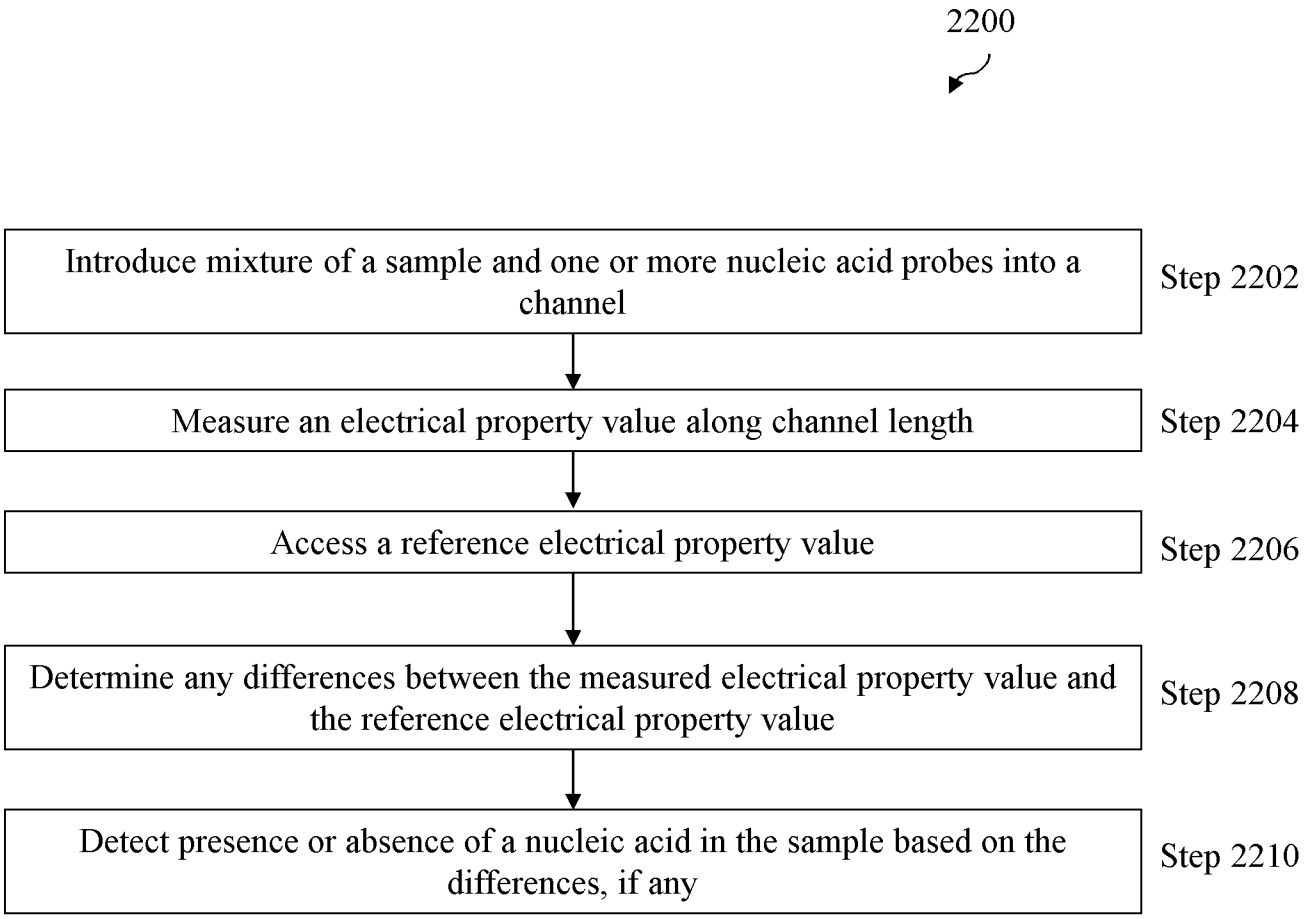

2200
Introduce mixture of a sample and one or more nucleic acid probes into a channel
Step 2202
Measure an electrical property value along channel length
Step 2204
Access a reference electrical property value
Step 2206
Determine any differences between the measured electrical property value and the reference electrical property value
Step 2208
Detect presence or absence of a nucleic acid in the sample based on the differences, if any
Step 2210

FIG. 22

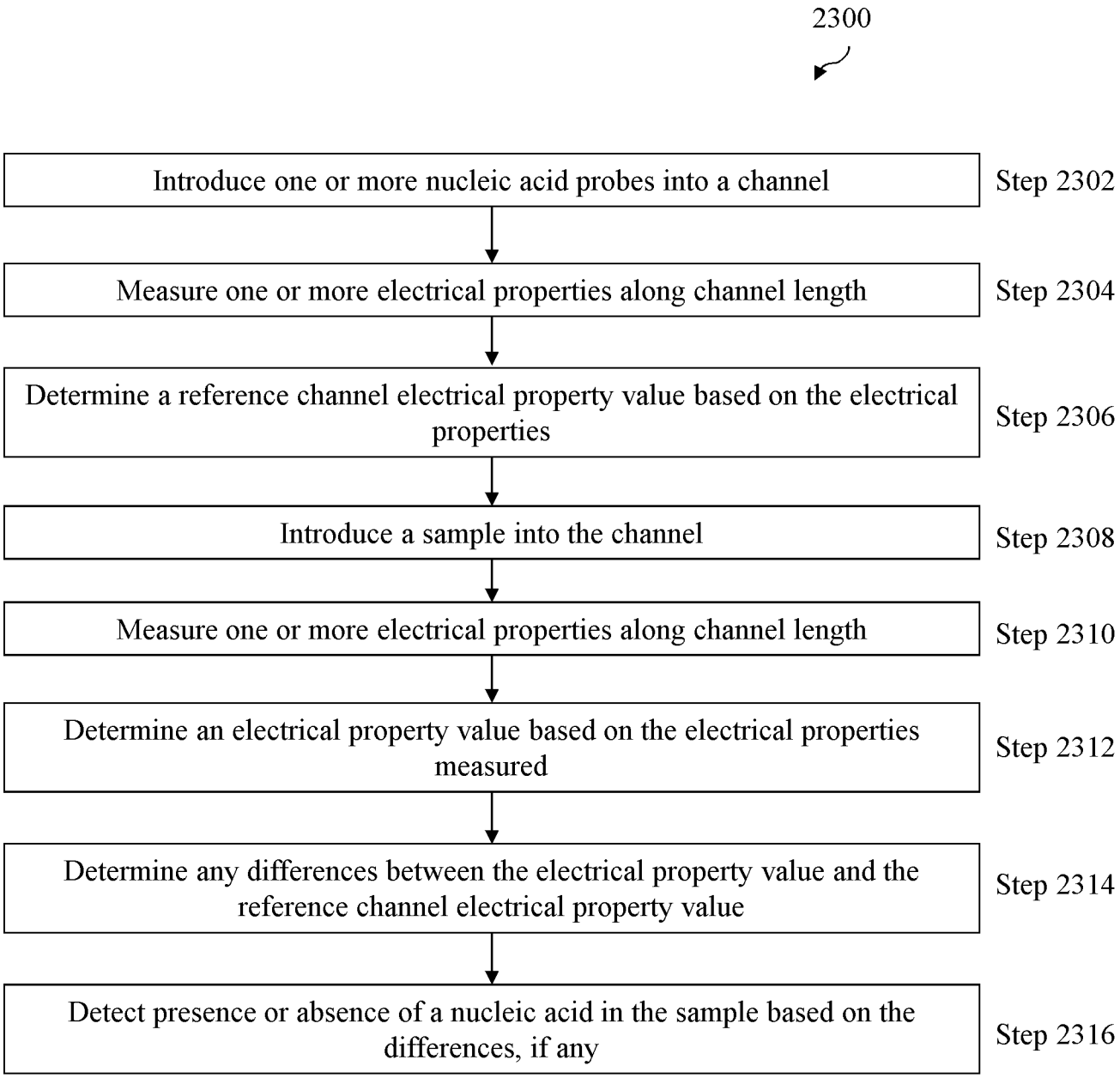

2300
Introduce one or more nucleic acid probes into a channel
Step 2302
Measure one or more electrical properties along channel length
Step 2304
Determine a reference channel electrical property value based on the electrical properties
Step 2306
Introduce a sample into the channel
Step 2308
Measure one or more electrical properties along channel length
Step 2310
Determine an electrical property value based on the electrical properties measured
Step 2312
Determine any differences between the electrical property value and the reference channel electrical property value
Step 2314
Detect presence or absence of a nucleic acid in the sample based on the differences, if any
Step 2316

FIG. 23

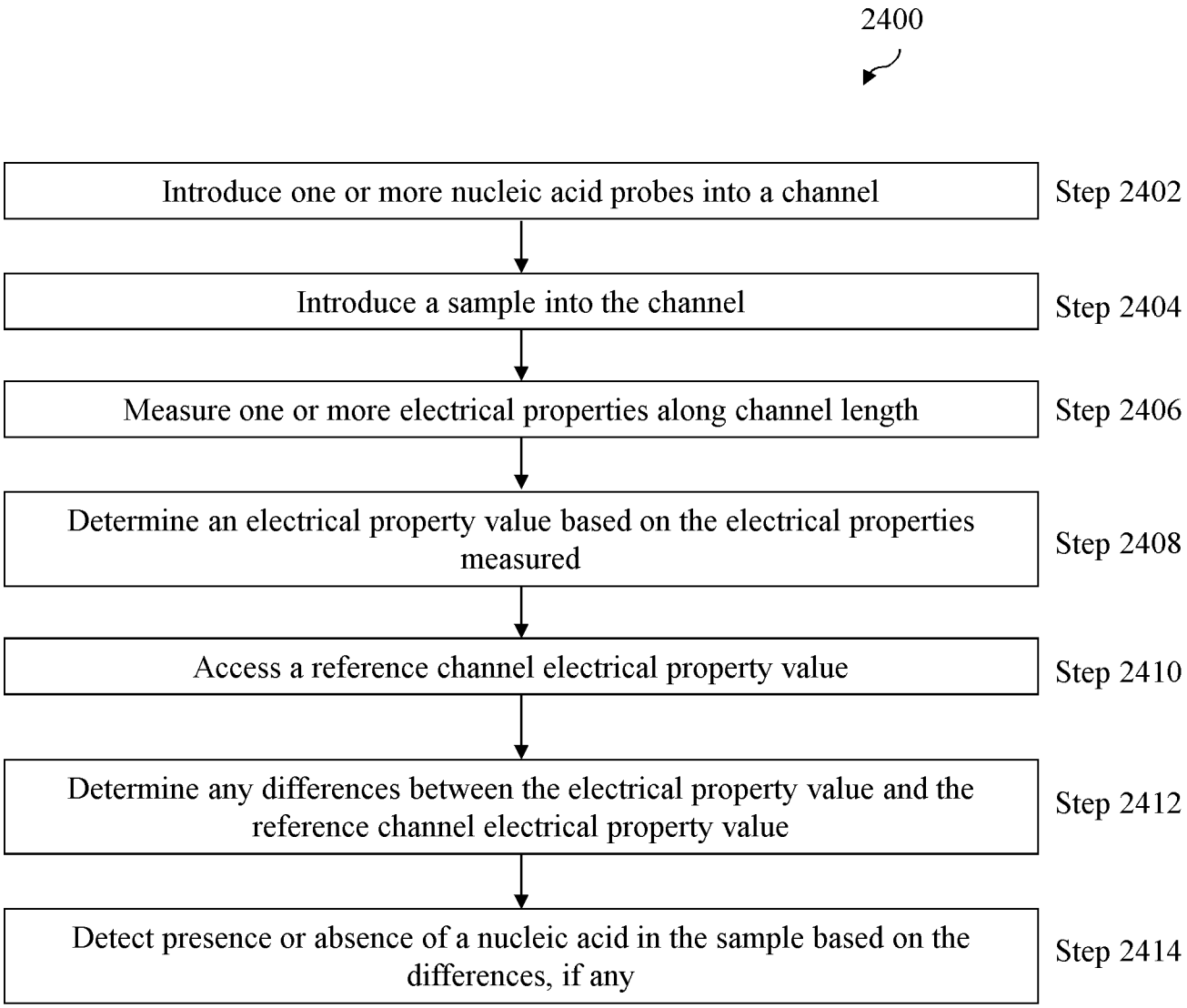

2400
Introduce one or more nucleic acid probes into a channel
Step 2402
Introduce a sample into the channel
Step 2404
Measure one or more electrical properties along channel length
Step 2406
Determine an electrical property value based on the electrical properties measured
Step 2408
Access a reference channel electrical property value
Step 2410
Determine any differences between the electrical property value and the reference channel electrical property value
Step 2412
Detect presence or absence of a nucleic acid in the sample based on the differences, if any
Step 2414

FIG. 24

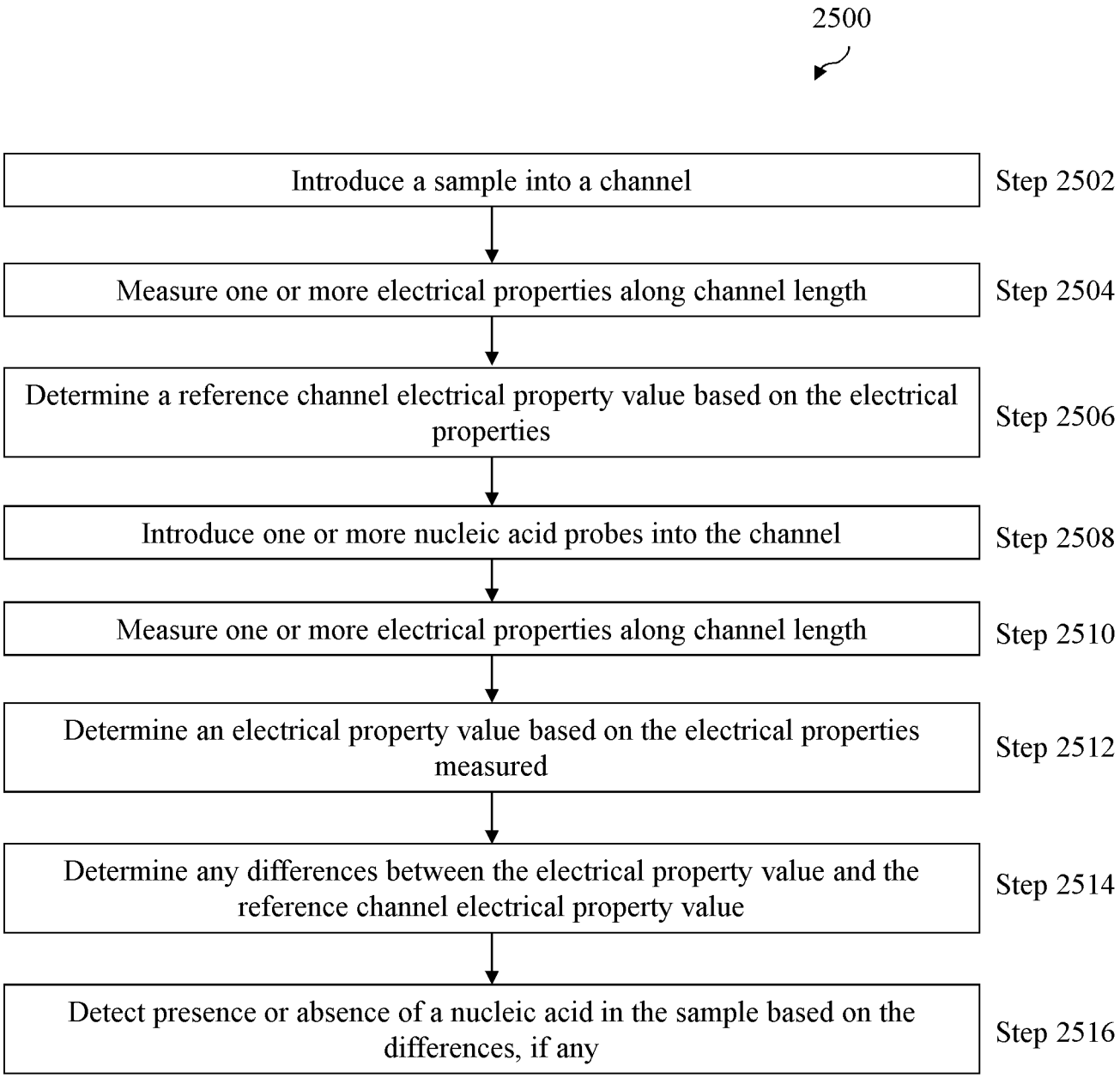

2500
Introduce a sample into a channel
Step 2502
Measure one or more electrical properties along channel length
Step 2504
Determine a reference channel electrical property value based on the electrical properties
Step 2506
Introduce one or more nucleic acid probes into the channel
Step 2508
Measure one or more electrical properties along channel length
Step 2510
Determine an electrical property value based on the electrical properties measured
Step 2512
Determine any differences between the electrical property value and the reference channel electrical property value
Step 2514
Detect presence or absence of a nucleic acid in the sample based on the differences, if any
Step 2516

FIG. 25

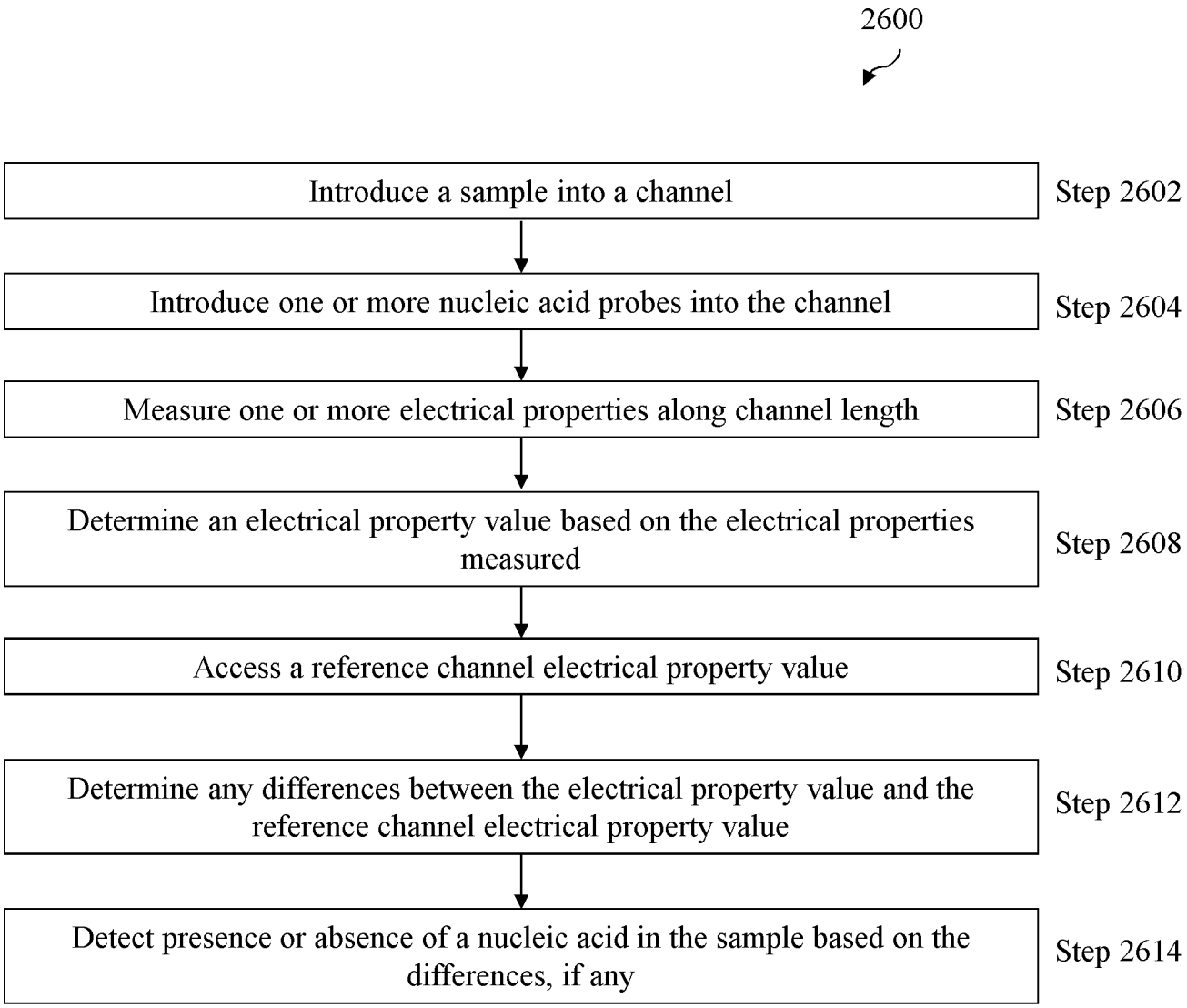

2600
Introduce a sample into a channel
Step 2602
Introduce one or more nucleic acid probes into the channel
Step 2604
Measure one or more electrical properties along channel length
Step 2606
Determine an electrical property value based on the electrical properties measured
Step 2608
Access a reference channel electrical property value
Step 2610
Determine any differences between the electrical property value and the reference channel electrical property value
Step 2612
Detect presence or absence of a nucleic acid in the sample based on the differences, if any
Step 2614

FIG. 26

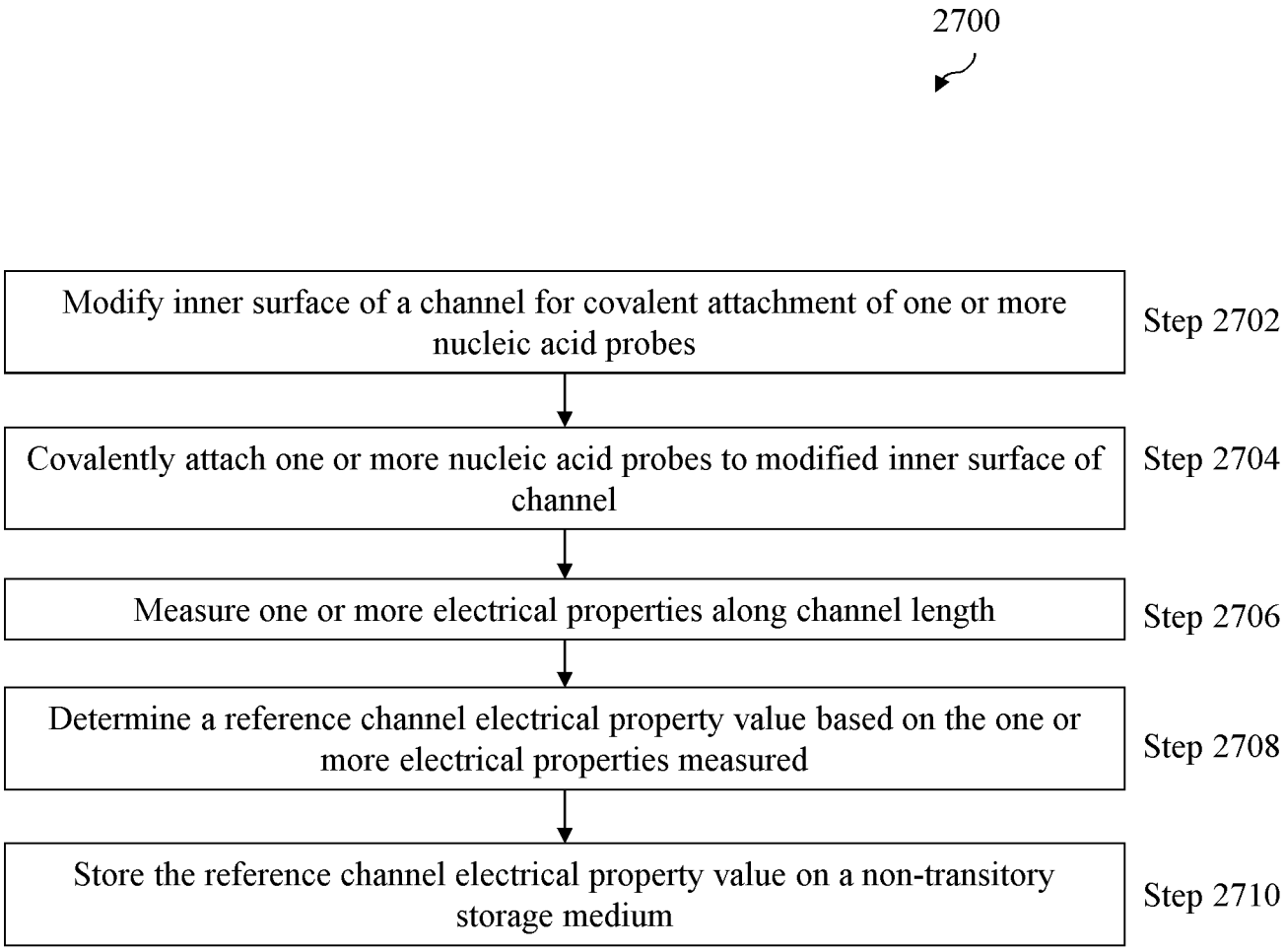

2700
Modify inner surface of a channel for covalent attachment of one or more nucleic acid probes
Step 2702
Covalently attach one or more nucleic acid probes to modified inner surface of channel
Step 2704
Measure one or more electrical properties along channel length
Step 2706
Determine a reference channel electrical property value based on the one or more electrical properties measured
Step 2708
Store the reference channel electrical property value on a non-transitory storage medium
Step 2710

FIG. 27

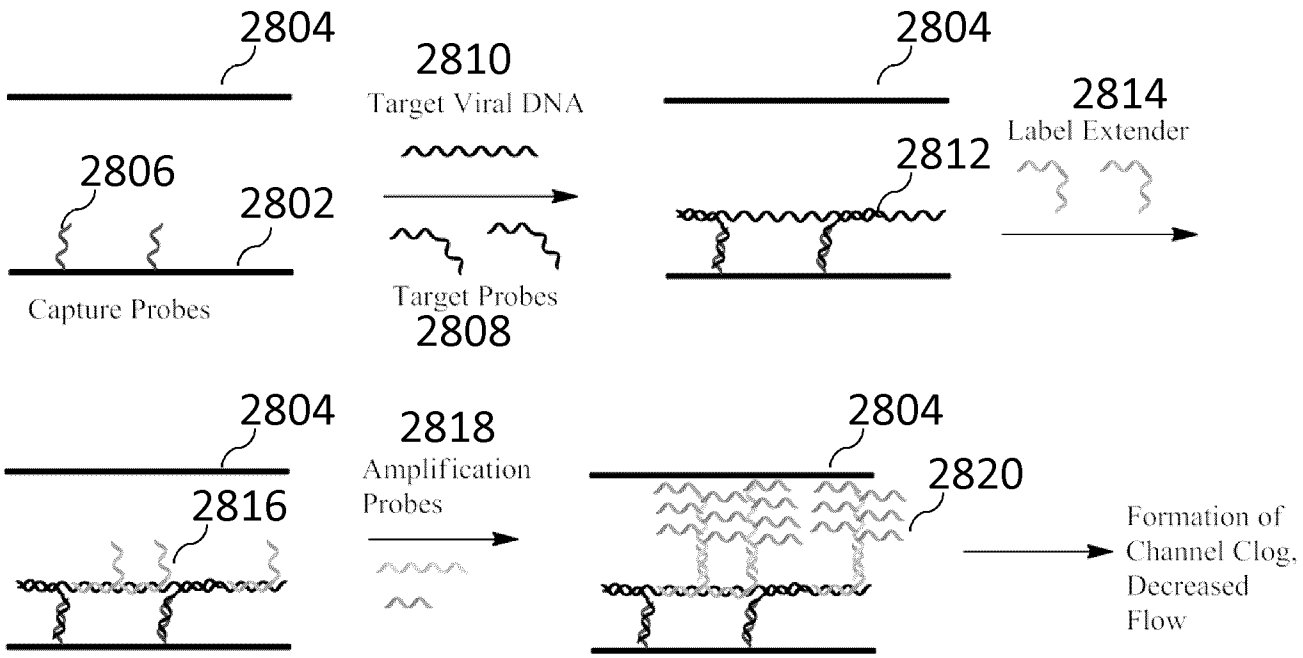

2804
2806
2802
Capture Probes
2810
Target Viral DNA
Target Probes
2808
2804
2812
2814
Label Extender
2804
2816
2818
Amplification Probes
2804
2820
Formation of Channel Clog, Decreased Flow

FIG. 28

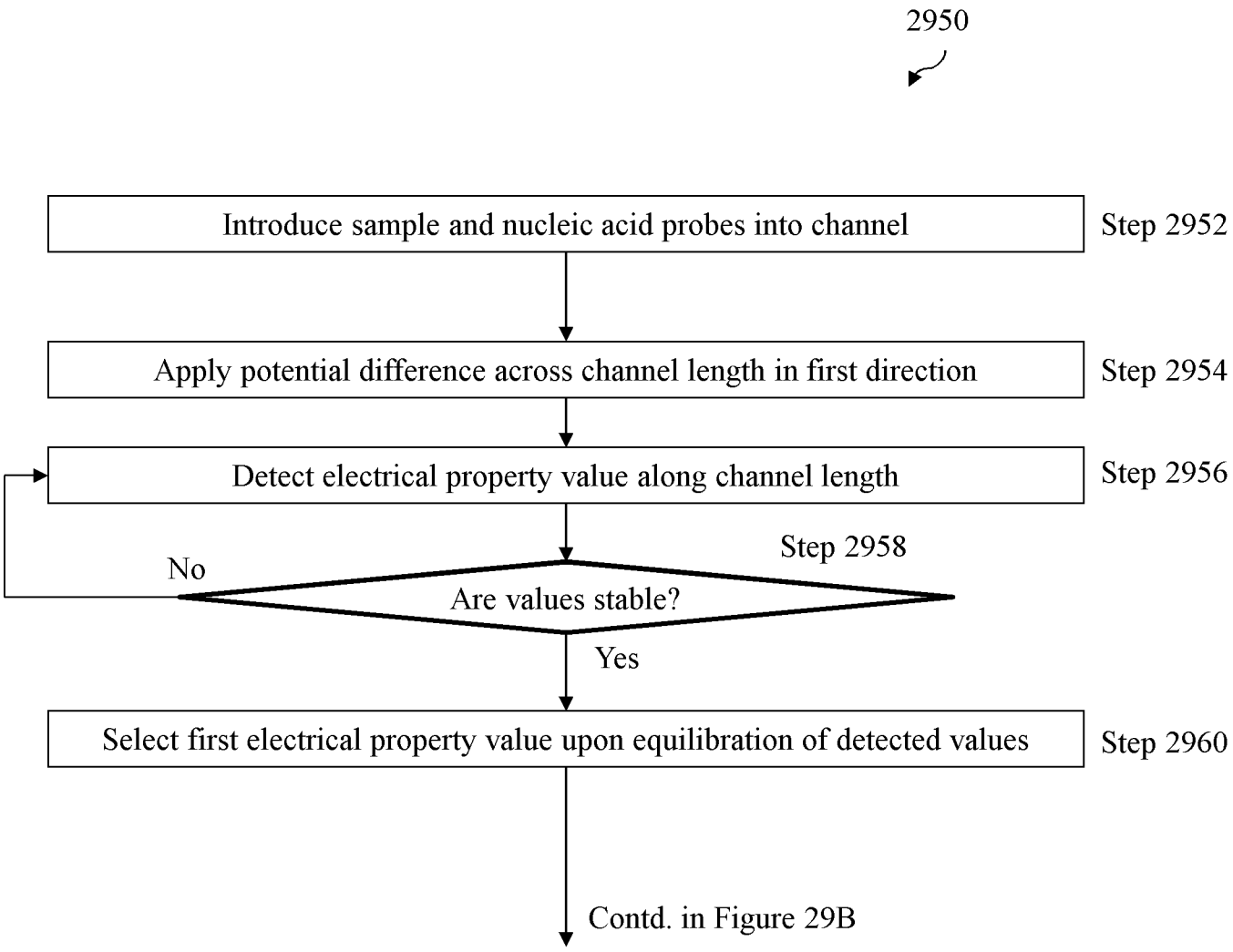

2950
Introduce sample and nucleic acid probes into channel
Step 2952
Apply potential difference across channel length in first direction
Step 2954
Detect electrical property value along channel length
Step 2956
Step 2958
No
Are values stable?
Yes
Select first electrical property value upon equilibration of detected values
Step 2960
Contd. in Figure 29B

FIG. 29A

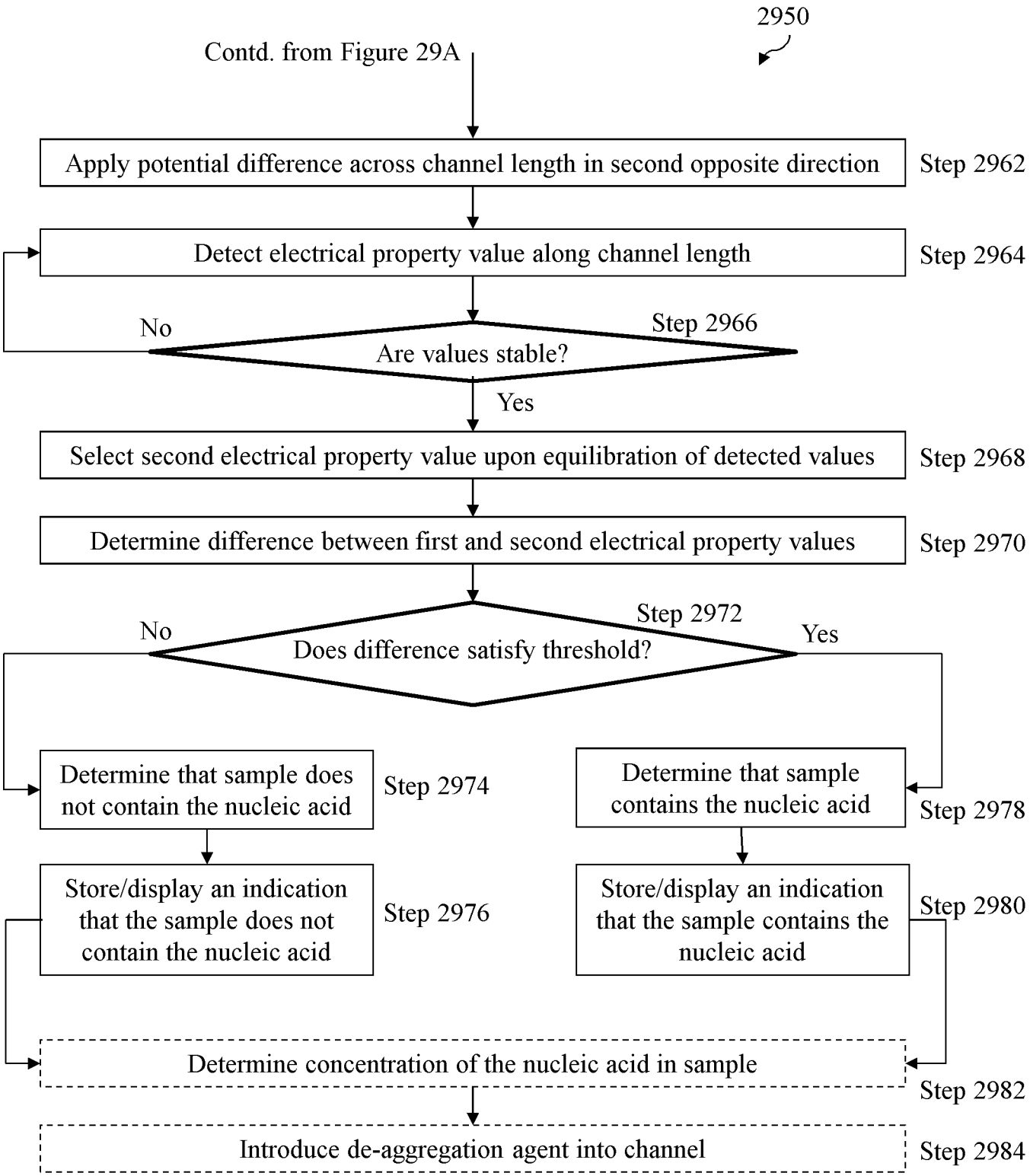

2950
Contd. from Figure 29A
Apply potential difference across channel length in second opposite direction
Step 2962
Detect electrical property value along channel length
Step 2964
No
Step 2966
Are values stable?
Yes
Select second electrical property value upon equilibration of detected values
Step 2968
Determine difference between first and second electrical property values
Step 2970
Step 2972
No
Does difference satisfy threshold?
Yes
Determine that sample does not contain the nucleic acid
Step 2974
Determine that sample contains the nucleic acid
Step 2978
Store/display an indication that the sample does not contain the nucleic acid
Step 2976
Store/display an indication that the sample contains the nucleic acid
Step 2980
Determine concentration of the nucleic acid in sample
Step 2982
Introduce de-aggregation agent into channel
Step 2984

FIG. 29B